UNITED NATIONS COLLABORATION IN THE SOCIOLOGICAL SCIENCES

SOME ten years ago Mr. L. V. Berkner, as special consultant to the Department of State, Washington, surveyed the Department's responsibilities in international science. The subsequent report, issued in May 1950 and entitled "Science and Foreign Relations", made numerous positive recommendations to promote the utilization of science in shaping national policy, including the establishment of a science office in the Department of State, the appointment of scientific attachés and measures to encourage the interchange of scientific and technical personnel and the flow of scientific and technical information. The report was discussed at the time in these columns (*Nature*, **166**, 81; 1950) and on subsequent occasions (for example, **170**, 1033; 1952), and the importance of its recommendations has become increasingly apparent with the growth of technical assistance programmes and of other measures to assist the under-developed countries.

In January 1958, the United States Committee on Foreign Relations decided to undertake a review of conditions and trends in the world, and of the relevant policies and programmes of the United States, prompted partly by the impact which Soviet scientific achievements might have upon the relations of the United States with the rest of the world. The inquiry then instituted developed later into a series of some fifteen studies of various aspects of the problem designed to provide a simple forthright statement of the basic aims of the foreign policy of the United States, which would reflect the motives and aspirations of its people, identify the forces which may frustrate or promote those aims, suggest means of controlling those forms and examine their impact upon the conduct of American foreign policy and the adequacy of the organization for determining such policy. The first of these studies, dealing with "Economic Problems and their Impact", was issued in August 1959, but the second, entitled "Possible Non-Military Scientific Developments and their Potential Impact on Foreign Policy Problems of the United States"*, is of as outstanding interest to the scientific and technical world generally as it is to those concerned with assistance to the under-developed areas of the world (to which one section of the report is devoted), and more especially with technical assistance, and it merits close attention as fully as the original Berkner Report.

This study was made by the Stanford Research Institute for the Committee on Foreign Relations, and explores, besides prospective scientific developments of the next decade and their potential impact on foreign policy, the possibility of making more positive use of science and technology. It does not except for brief discussion, deal with possible scientific contributions to problems of disarmament or examine developments in military technology; nor does it deal further with matters such as scientific attachés, the promotion of scientific exchanges and the support of scientific activities overseas, with which the Berkner Report itself was concerned. Broadly, the report points out that while scientific developments may help to solve some problems of foreign policy, unless deliberate measures of policy are taken, the progress of science and technology will do more to create or intensify than to solve such problems. In the absence of such measures, the combination of pressures may easily lead to their relief by the traditional methods of war, famine and disease. The great danger is complacency, for under present allocations of effort to research and the diffusion of results, the urgency of the problems is likely to increase faster than the means of solving them.

The national interest of the United States thus requires a more conscious direction of scientific activity in ways which promise to assist in attaining the country's international objectives. In other words, security and welfare themselves call for a re-appraisal of present allocations of scientific and technical effort so as to increase that directed toward meeting the non-military challenges of foreign policy. The report suggests that the Committee on Foreign Relations could take steps to stimulate additional research and development directed specifically at important problems in that field, and indicates particular types of problem which call for such attention. It also suggests that steps could be taken to double or triple the amount of fundamental scientific research in fields where progress in scientific understanding is particularly important to foreign policy, and that the Committee should encourage the international proclivities of science and scientists to build bridges of understanding. Concrete suggestions include more international scientific conferences and interchange of personnel, international research programmes, an international centre for translation and scientific information, a world-wide attack on the problems of economic and social development in an 'International Development Year', and a lead in establishing a United Nations university. Foreign policy planning of the broadest kind, utilizing the best scientific assistance, will be a critical requirement in the years ahead, and this should include continual review of prospective scientific developments and their significance for international relations.

In this report the relations between scientific developments and foreign policy are discussed in the first chapter, including both the way foreign policy has been affected in the past, the nature of the connecting links and the possibilities both of anticipating

* United States (86th Congress, 1st Session). United States Foreign Policy. Possible Nonmilitary Scientific Developments and their Potential Impact on Foreign Policy Problems of the United States. Study prepared at the request of the Committee on Foreign Relations, United States Senate, by Stanford Research Institute. Pp. ix+100. (Washington, D.C.: Government Printing Office, 1959.)

and shaping scientific developments. The second section, dealing with future problems of foreign policy in the light of scientific developments, which in successive chapters covers science and national sovereignty; population, food and science; science and the under-developed countries; energy, materials and trade; and science and international communications; it approaches these problems primarily but not exclusively from the point of view of the United States. Nevertheless, like the section on future policy, where the positive use of science to achieve international goals is more particularly considered, it contains much that is fully relevant to those concerned with science and with foreign policy in other countries, and the whole report deserves the closest attention not only of the Secretary of State for Foreign Affairs in the United States but also of the Minister for Science and the Advisory Council for Scientific Policy in Great Britain. The picture displayed of the immense array of complex interlocked problems calling for urgent action applies fully as much to Britain, and it may be even more imperative for both the security and the welfare of Britain that the right priorities should be determined and our limited resources applied in accordance with them.

This is especially evident in the chapter of the report which considers the positive use of science to achieve international goals. The evidence presented there of the accelerating rate of discovery and invention applies generally. All over the world the number of scientists and technologists is rapidly increasing, and also expenditure on research and development. The increasing efficiency of diffusion of new ideas and techniques, and the more powerful tools of investigation available to scientists and technologists, act in the same way as does the expansion of organized team-work and the more favourable social attitudes, while to-day international competition and emulation tend to spur scientific and technical development and could easily do so in ways wasteful of the world's resources. Nevertheless, there are fields in which scientific effort is still undesirably low, and the report remarks on the effort specifically directed towards the peaceful achievement of objectives of foreign policy and the basic problems of human relations and social organization, including international aspects of such problems.

The report, in discussing next the positive use of science, makes some specific suggestions regarding non-military aspects of problems of foreign policy in which insufficient attention has been given to the possibility of attack by adequate fundamental research in the relevant sciences. It suggests, for example, that a responsibility should be established within the Government for continuing review of prospective scientific developments and their impact on foreign policy. In Britain, this would now appear to rest unequivocably with the Minister for Science and the Advisory Council for Scientific Policy. More specifically, the report quotes problems in oceanography, the polar regions, the atmosphere and space research, but stresses the need to include also studies of a legal, political and administrative as well as physical and biological character. Again, it is asked whether sufficient positive use of science is made in developing and adapting promising methods of improving food production, making the most effective use of American surpluses and exploring the possibilities of population control. Next, there are problems of planning for new world relations in production and trade, such as assessing the new competition and market opportunities likely to result from the spread of modern technology to the formerly under-developed countries, or the possibility of making long-term analyses of world supplies of raw materials and energy, and of world trade patterns. Problems of communication with other nations provide another set of problems in social science, and there are others of international political organization, law and administration where further research on political systems and legal and administrative systems might disclose the best ways of strengthening the United Nations and advancing towards a world rule of law.

In two particular sections, the report deals at greater length with the possibilities of action and the range of problems presented. First, in the matter of arms control and disarmament, besides the technical problems of control of armament and the devising of systems of inspection to prevent violation calling for constant research, the economic repercussions and adjustments should be explored, so that the individual nations are ready to deal with the consequences should a substantial measure of disarmament become possible. The report emphasizes the need for a continuing study, adequately financed, to deal with such technical problems as observation techniques, including radar, aerial photography, ground observers, seismic means for monitoring nuclear explosions, problems involving communication and data-processing systems.

Secondly, the development of under-developed countries presents a wide range of problems in which specific research is likely to assist materially. The report mentions simpler and cheap power sources for villages and towns, including electrical generators from local resources, gas from agricultural wastes, etc., wind-power, solar energy, storage of energy and small nuclear power stations. Improved but simple and cheap housing materials and constructional methods offer other possibilities, as does water supply for irrigation and industrial use, for example, by cheap desalting processes. Simple, cheap methods of refrigeration for foods and cooling of houses; environmental sanitation; the control of special diseases, such as hepatitis, filariasis, brucellosis, trachoma, dysenteries; food preservation; the improvement of food crops and animals; and the control of the growth of population—all these present physical science with urgent research problems.

Attention is also directed to the range of problems in sociological and social research presented by the improvement in techniques of planning development programmes, by development of simple, cheap methods of mass education, the diversity of methods of introducing agricultural and rural improvements,

communicating effectively with people, and inducing them to adopt better practices. Methods of introducing modern industrial techniques and meeting problems of industrialization, and government methods compatible with democratic ideals but more suitable to the special circumstances of the under-developed countries, offer another fruitful field for such research, and much emphasis is laid not only on the need for fundamental research in the physical, as well as in the pyschological and social sciences, but also for better theories. The major need, it is asserted, is for better interpretation of the facts, better understanding of their meaning in terms of our aims, ideals and plans, and for better founded notions about the probable effects of one course of action or another.

It is not suggested in the report that simple solutions to these problems are likely to be found, but there is sound sense in the argument that it is at least possible that imaginative, carefully designed basic research could eventually throw light on the soundness of even such a difficult problem as the foundations of the psychological assumptions of the theory of deterrence on which much of the Western policy for preventing nuclear attack is based. Excluding the military aspects, the problems of foreign policy are overwhelmingly human ones, and the psychological and social sciences, to which the makers of foreign policy should be able to, and, to a significant extent do, look for insight and help, are the least well developed and least well supported of the major scientific groups. Without expecting quick and easy solutions to problems of human relations, there is ample basis for believing that more effort in this field could lay the foundations for much better understanding of the nature of some of the problems that arise in foreign policy and considerably help those who make it. The president of Stanford Research Institute, Mr. F. Finlay Carter, unhesitatingly affirms his belief that research can make many contributions to the better understanding of the invisible but very real forces affecting human behaviour, human relations and human institutions.

In view of the establishment last year in Britain of the Overseas Research Council, it is interesting to note that the report suggests that the United States Government should be provided at some appropriate point with an office of research and development concerned with problems of under-developed areas, and that such an agency could initiate a systematic programme for identifying problems where scientific and technological discovery could assist to accelerate development and that it could then stimulate research on these problems, either in the United States or abroad. Even in the physical sciences, the problems of this type are in some way or other neglected in the post-war world; and it is obvious that their solution must involve some redistribution of resources.

That is one sound reason for advocating that the attack upon them, where possible, should be made by international agencies; and not the least important section of this highly suggestive report is that where, in conclusion, it discusses the possibility of encouraging the tendencies of science and scientists to work across national frontiers to build bridges of understanding between East and West—between the under-developed and the industrially advanced nations. The value of scientific conferences and the interchange of scientists and scholars at all levels is recognized in the first place, and some stress is also laid on the contribution which advances in mechanized translation and information facilities could make both by improving communication between scientists and reducing the language problems of mankind. Moreover, it has already been widely recognized that some of the fields of research to which the report directs attention can be prosecuted to advantage by international agencies or by the co-operation of research institutions in several countries. Examples are to be seen in oceanography, polar and space research, and the atmosphere; and the report of the International Council of Scientific Unions indicates not merely that a start has already been made, but also something of the possibilities, given substantial financial backing and goodwill. Arctic and deep-sea research are instanced as further possibilities which merit examination, and also the establishment of a United Nations weather and climate agency.

The proposal regarding the under-developed countries already noted deserves special attention as indicating a novel approach to a problem of growing urgency and importance. The International Development Year suggested would initiate, much on the lines of the International Geophysical Year, fundamental new studies on an international basis on the key development problems of under-developed countries, and would stimulate the fundamental research in these aspects of the physical, biological, psychological and social problems from which contributions to the solution of these problems might be expected. The United Nations university scheme, which, it is suggested, the United States might also take the lead in establishing, would possibly include a World Institute of Social Technology, for advanced research and teaching in the practical application of psychological and social science to problems of human relations and social organization, especially where they bear on these problems; but the major purpose of the university scheme would be the advancement of science and the humanities, and thereby the discovery and development of the unifying elements in the human values widely held by the different groups and cultural traditions of mankind. It is suggested that the system might be financed by an annual contribution of 0·1 per cent of the annual expenditure of each member of the United Nations on military defence, or an agreed fraction of the index of the total national product.

No reader of the report is left in any doubt as to the danger of failing to give much greater attention to the significance of scientific and technological advance for national policy, including foreign policy, or as to the improbability that an adequate attack can be made on many of the problems now confronting us except on an international basis. The

facts that the creation of a Minister for Science and the existence of an Advisory Council for Scientific Policy in Britain, together with the clear recognition that Britain's contribution to space research should be made on an international basis, place this country in an advantageous position to co-operate in this way, is no ground for complacency. The suggestions made in this report and their implications deserve to be closely considered by the Minister for Science, the Advisory Council for Scientific Policy and the Overseas Research Council at least, with a view both of increasing our present effort and ensuring that it is concerted as effectively as possible in co-operation with that of other nations.

POST-MORTEM ON GROUNDNUTS?

Agriculture and Ecology in Africa

A Study of Actual and Potential Development South of the Sahara. By Prof. John Phillips. Pp. 424. (London: Faber and Faber, Ltd., 1959.) 63*s*. net.

POLITICAL advances in tropical Africa can only be successful if economic progress is accelerated. Industrial developments are important, but for many years agriculture in one form or another will be the major industry of all the countries in Africa south of the Sahara. Today agricultural progress is slow, and where crops have brought prosperity, as cocoa has to Ghana, this is because the price has risen disproportionately to the rise in other world prices, and not because the yield has risen substantially. Unless methods of agriculture in many countries are greatly improved, as the population increases even the present pitifully low standards of living will be difficult to maintain.

Prof. Phillips's book is about this problem. He has been himself concerned with ecological and agricultural works in many parts of Africa for nearly forty years. He was the botanical ecologist in Swynnerton's team of tsetse fly investigators in Tanganyika. He was professor of botany at the University of the Witwatersrand. He was one of the senior scientists concerned with the ill-fated East African groundnut scheme. Since 1952 he has been professor of agriculture in the University College in Ghana. Few men can have seen so much of African agriculture, and have been made so aware of its problems.

In this book an immense amount of information about the climate, soil, crops and people of Africa is brought together. It must have been a tremendous task for the author to make this compilation, and his book will at least serve as an invaluable work of reference to those unable to go to the original sources. I do not think that it will succeed so well in its avowed purpose "to awaken those concerned with Africa to the necessity of adjusting both traditional and modern agriculture to the ecological, sociological and psychological settings of the Trans-Sahara".

The first disadvantage of this volume is that it is so difficult to read. The (very valuable) data are set out at length, usually undigested, and I found I could only assimilate those in which I had some particular and personal interest. Between the data the reader is treated to infuriating examples of flowery prose in Prof. Phillips's own particular style. In one paragraph three consecutive sentences start: "Sketchy is the information . . .". "Essential is the need . . .". "Unnecessary is a review . . .". We are, however, left with a true picture of Africa, vast, varied, and (in the main) unproductive; but this could have been much more easily achieved and with less strain on the reader.

What should have been the most valuable chapter compares three large-scale development schemes. These are the Sudan Gezira Scheme, the East African Groundnut Scheme, and the proposed Volta River Project in Ghana. We are shown how fundamentally different the conditions for the successful Gezira Scheme and the groundnut fiasco were, but instead of a straightforward account of each we are treated to a point-by-point comparison of features which are not always strictly comparable. We can in the end only conclude that in the Gezira conditions were favourable, and in Tanganyika everything was done in too great a hurry.

It is difficult to imagine how this book can have any important and practical results. We are told that agriculture must be ecological, which simply means that we must learn to grow the correct crops by the best methods in the best places. We are not told how to do this, except that we must not be in too much of a hurry, and that research must be properly co-ordinated.

In my opinion the trouble with African agriculture is not that information is not properly co-ordinated, but that the basic facts are simply not known. So little fundamental agricultural research has been done. Even in Britain we spend more in subsidizing our poultry industry for a month than we spend on agricultural research in a year; in Africa, with its immense areas and problems, we spend much less. Even attempts at developments like the Groundnut Scheme, into which millions of pounds were poured, seem less wasteful when it is realized that for every pound lost in this and in all agricultural schemes attempted in Africa since the War, much more than a hundred pounds has been spent in subsidizing British agriculture at home. More money will have to be spent on research in Africa. We need to have more and better research workers in the laboratories and in the field; I believe they will use the limited resources better than those who fritter away so much time and money attending international conferences and endless meetings of co-ordinating committees which lack the basic facts to co-ordinate. If the newly independent territories in Africa can learn this lesson, and develop an environment favourable to working scientists (expatriate as well as local), there is a reasonable chance that they may learn to take proper advantage of the ecological conditions of their countries in agriculture as in other fields of development.

KENNETH MELLANBY

CHANGING COASTLINES

Beaches and Coasts

By Dr. C. A. M. King. Pp. xii+403. (London: Edward Arnold (Publishers), Ltd., 1959.) 65*s*. net.

IT is now forty years since the publication of D. W. Johnson's pioneer and now classic work "Shore Processes and Shoreline Development". In the meantime much work has been carried out, both theoretical and practical, on the processes at work along the coasts and the evolution of different types of shoreline. Problems of coast erosion and, equally, of coastal

accretion have long been matters of much concern to civil engineers who, in the absence of precise investigations, were compelled to use empirical methods. Work in recent decades has been full of surprises. Though the widespread occurrence of steep-sided offshore canyons around the coasts is one of the surprises, this lies beyond the scope of the present work, where a beach is defined as an accumulation of loose material around the limit of wave action—extending through a zone divided into backshore, foreshore and offshore, from the extreme upper limit of wave action to the depth at which waves approaching from deep water first cause appreciable movement of the bottom materials. This scholarly, well-documented treatise first defines the four main factors on which the character of a beach depends, namely beach material, waves, tides, winds. It then considers briefly the three parallel methods of research—theoretical, experimental (especially wave-tanks such as that long in use in the Department of Geography at Cambridge) and field observations. A fourth approach, the historical, is mentioned, but sufficiently detailed information is rarely available. The main topics are then taken up in the order of waves, movement of material, beach profiles, effect of wind, classification of beaches and coasts, constructive and destructive wave action, and, finally, the marine cycle. Examples are drawn from world-wide sources with a particularly thorough examination of all the work around Britain.

Every point is substantiated by appropriate references, and nowhere is the reader left with the impression that all is adequately known and understood. Instead, the memory of the disastrous coastal floods of 1953 is still fresh in England; what may prove to be the tragic mistake of closing to scientific research the great natural laboratory of Dungeness is within the last few months. There is no doubt that protective works in one area have unexpected results in another; if half a million acres of tidal flat are awaiting 'reclamation', as some would claim, it is vital to know what will be the consequences elsewhere. The field of study covered in this book is part of the important new field of applied geomorphology. It is perhaps inevitable, if regrettable, that a new 'jargon' should arise that one needs to study the dilatancy and thixotropy of sediments. But perhaps the deliberate creation of new words is safer than the attempt to define by size granules, pebbles, cobbles and boulders, or to insist on new exact meanings for berm and runnel.

L. Dudley Stamp

PRECIS OF PROGRESS IN BIOCHEMISTRY

Progress in Biochemistry

A Report on Biochemical Problems and on Biochemical Research since 1949. By Prof. Felix Haurowitz. Pp. xii+357. (Basel: S. Karger; New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1959.) 60*s*.; 8.50 dollars.

THE fifth in Prof. Haurowitz's series of reports on progress in biochemistry deals with the advances in this field since 1949, and we gather from the author's foreword that he was hesitant to prepare it. He comments that "limits of time and human endurance make it more and more difficult to grasp, let alone to master, the entire field of biochemistry". This *cri de cœur* will surely find an echo in many laboratories and lecture rooms, and for this reason alone, quite apart from the book's intrinsic merits, it is likely that Prof. Haurowitz's courage and virtuosity in grappling with the smothering excess of the printed word will earn the reader's gratitude.

But his claim to our thanks is more firmly founded for there can be no doubt that, within his terms of reference, he has written a most useful book, which gives fluent accounts of the progress made in all those aspects of the subject normally dealt with in the standard text-books. His method has its own particular merits: thus, except where a brief reminder may help the correlation of recent advances with established work, it is free from the necessity of giving the repetitious background to knowledge which necessarily swells each general text-book in turn. On the other hand, because it reports the work of a decade it is frequently able to focus topics which an annual review sees only as the indistinct blur of work-in-progress; moreover, it is spared the uncritically comprehensive list of references which can so effectively throttle the text of more definitive reviews. In ten years a measure of sifting becomes possible, and the references retained and commented upon here seem to have been chosen with excellent discrimination.

Taken on this level, therefore, as a series of timely supplements to the general text-books, these volumes may be judged to have introduced successfully a new style of reporting into biochemistry. Necessarily they risk the defects of any anthology; there may be omissions and faults of emphasis. But it is certain that most readers will find new and stimulating expositions in the pages of this latest volume, and even be led to an appreciation of new aspects of the subject which had lain unregarded by them in the more specialist literature.

F. H. Malpress

APPLIED MICROBIOLOGY

Advances in Applied Microbiology

Vol. 1. Edited by Wayne W. Umbreit. Pp. xi+304. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1959.) 9.50 dollars.

THIS volume is presented as the first of a projected new series of reviews on microbiological topics of interest to the practical microbiologist. Applied microbiology is, in its widest sense, a subject that covers or overlaps considerable areas of present-day scientific research. In recent years the synthetic and degradative powers of micro-organisms have been increasingly harnessed in the laboratory and factory, as microbial synthesis has often proved the only convenient method of preparing a number of compounds important in pharmacy or nutrition.

Three chapters are on general problems of large-scale fermentation: P. Gerhardt and M. C. Bartlett classify the types of continuous fermentation and consider their theoretical basis and practical applications, M. Herold and J. Nečásek discuss the value of the use of antimicrobial agents to control contaminating micro-organisms that interfere with industrial fermentation processes, and R. F. Robinson and R. S. Davidson give an interesting account of the problems

attending the large-scale production of edible fungi and urge greater consideration of the use of the higher fungi to convert carbohydrate-containing wastes into foods rich in fat and protein. In the three articles concerned with the use of micro-organisms as synthetic tools D. Perlmann gives a comprehensive and fully documented account of the biosynthesis of vitamin B_{12} and its analogues, A. L. Demain contributes a critical discussion of the biosynthetic pathway leading to penicillin, with particular reference to the synthesis of the β-lactam-thiazolidine ring nucleus, and S. Kinoshita introduces the new and rapidly developing field, largely pioneered in Japan, of amino-acid production by fermentation processes.

Articles dealing with the control of micro-organisms include a discussion of the antimicrobial activity of phenols by E. O. Bennett, a brief review of the use and mode of action of antibiotics in the control of plant diseases by D. Pramer, and a general outline of some of the problems associated with the application of radiation preservation to food and pharmaceutical products by W. D. Bellamy. A. W. Phillips and J. E. Smith trace the development of the methods used for the rearing of germ-free animals, list their characteristics and consider some of the many uses to which such animals have been, or can be, put. In the remaining chapter, S. R. Dutky contributes a valuable discussion of the application of specific micro-organisms in the control of insects, a procedure that eliminates many of the hazards to plants and animals presented by the use of insecticides.

The eleven chapters in this book deal with a representative selection of topics, and the diversity of the subjects is no doubt responsible for some of the differences apparent in the level of treatment in individual articles. The book is well presented, adequately indexed and should surely be welcomed as the first of a useful series.

J. W. G. Porter

TRAINING APPRENTICES

Apprenticeship

An Enquiry into Its Adequacy under Modern Conditions. By Kate Liepmann. (International Library of Sociology and Social Reconstruction.) Pp. x+204. (London: Routledge and Kegan Paul; New York: The Humanities Press, Ltd., 1960.) 23*s*. net.

FOR two years a small group of investigators from the University of Bristol made an inquiry into systems of apprenticeships in firms in the Bristol area and in an agricultural area in North Somerset. Information was obtained from both the managerial and trade union sides of industry, as well as from technical colleges and relevant Government departments. Dr. Kate Liepmann was directly responsible for the study and here sets down details of the way the inquiry was made and a record of the findings.

The industries investigated—engineering, printing and building—were selected because of their local importance and because of significant differences in apprenticeship conditions, degrees of mechanization, 'de-skilling' and attractiveness to boys. An industry without apprenticeship, boot and shoe manufacture, was included for comparison. Most of the firms approached readily provided the information requested by the investigators. One large printing firm refused any information after a preliminary interview. Another big printing firm and the area's biggest engineering firm allowed the research workers access to certain senior executives but to no other employees. Information from these was obtained in other ways, but the omissions detracted from the value of the survey.

There is no reason to reject Dr. Liepmann's belief that the observations made during her Bristol survey would not be applicable to Britain as a whole. Its value is that this is an investigation carried out by professional research workers with no axe to grind, holding allegiance neither to employers, trade unions, technical college principals, nor Government agencies, and concerned only to record their findings quite impartially.

From the nation's point of view the scene described is depressing to contemplate. Instead of a means to build up the quality of human beings and to increase the country's resources of skilled craftsmen, the apprenticeship system is used by both sides of industry to further their respective sectional interest. "All the modifications made in adjustment to technical and other developments have been made in such a manner as to preserve the power of employers and trade unions to bend apprenticeship to their own ends".

The criteria for judging the workings of the apprenticeship system should be examined to see whether it supplies sufficient workers with the requisite skills, is efficient and economical to operate, and its effect on productivity. Dr. Liepmann's investigations show that industry is not training nearly enough apprentices with a wide degree of skill which will enable them to adapt themselves to changing technological needs. Nearly every firm looks after its particular interest and many of them rely on 'poaching' craftsmen from other firms to supply their needs. She rightly concludes that it is not in the best interests of the community that the number of apprentices should be determined by industry itself.

As a contribution to productivity the apprenticeship system leaves much to be desired. Although, as part of their training, apprentices make some contribution to productivity, the apprenticeship scheme leads to a widespread system of restrictive practices; rigid demarcation between trades impedes good manpower utilization, thereby lowering efficiency and increasing the cost of production: and, unfortunately, the demarcation which was formerly exclusive to apprenticed craftsmen is now being extended to a much wider class of workers, with further damage to productivity.

Despite the hope that some developments in the trade union movement may lead to the emergence of an attitude more in line with modern conditions, Dr. Liepmann concludes her inquiry with the firm belief that the State should take the prime responsibility for training for industry, both in its quantitative and qualitative aspects.

This is the second of two recent studies of the workings of the apprenticeship system by academic workers. Their observations are almost identical and should cause wide-spread concern. If the Ministers of Labour and of Education could be persuaded to read this or Lady Williams's book, they would see that the exhortations to industry of their predecessors have been so much wasted breath. Without a change in policy for the training of young workers, within twenty years Britain may face grave shortages of skilled and adaptable craftsmen.

Out of Doors

Edited by Winwood Reade. Pp. 160. (London: Rathbone Books, Ltd., 1959.) 12*s*. 6*d*. net.

"OUT OF DOORS" is a book written specially for children with the purpose of catching their interest and encouraging their observations of wild life. It cannot fail to do either. By dividing the book into twelve chapters, one for each month of the year, it provides a perpetual stimulus.

Under each month there are four sections. The first deals with things that can be seen out of doors. A large number of general facts are given here, as well as the specific observations for the particular month. The easy style and abundant illustrations of this first section set the tone for the rest. Secondly, there is an excellent article on one particular topic, written by a well-known naturalist. The third section of each month describes, very simply, something practical that can be made, done or collected. The last section is always two picture puzzles. These may be difficult for children; but even if they do not actually know the answers they will enjoy guessing, and learn something by looking up the correct answers in the back of the book.

The book combines all the qualities that enable a child to learn enjoyably. Not only is it highly informative, and infectious in its enthusiasm for the subject; it also appeals to a child's love of practical work, and encourages him to use his eyes. These qualities make "Out of Doors" suitable for even the young child. At the same time, many adults will be more than pleased to widen their knowledge of birds, trees, flowers, insects, animals, etc., in such a straightforward manner.

There are no coloured plates, which one misses, perhaps, in a book of this kind, and which always catch the eye, but this is more than made up for by the numerous excellent black-and-white illustrations.

B. J. G. MAITLAND

The Waterfowl of the World

By Jean Delacour. Vol. 3: Eiders, Pochards, Perching Ducks, Scoters, Golden-eyes and Mergansers, Stiff-tailed Ducks. Pp. 270+20 plates. (London: Country Life, Ltd., 1959.) 126*s*. net.

WITH this third volume Mr. Delacour completes his account of the ducks, geese and swans of the world; we thus now have a comprehensive modern work on the Anatidae by a recognized authority, with Mr. Peter Scott's colour figures of the birds in their various plumage phases and useful distribution maps. The information given for each species or sub-species covers description, distribution, general habits and record in captivity—this last of special interest to the aviculturist.

Vol. 3 begins with the eiders, including the familiar British species. It proceeds to the pochards, narrow-billed and broad-billed respectively. Next come the perching ducks (or tree ducks), including the Carolina wood-duck so familiar in captivity and the beautiful mandarin duck which has lately become feral in England; the rest are tropical, including the so-called pygmy geese, the unique comb duck, the spur-winged goose, and the muscovy duck—the last a South American species which has been domesticated and is often crossed with the domestic mallard. Then we come to a group which includes such largely marine diving ducks as the scoters and golden-eyes and also the saw-billed ducks or mergansers. Finally there are the stiff-tailed ducks, including the strange musk duck of Australia and the aberrant black-headed duck of South America, which has the cuckoo-like habit of foisting its parental duties on other species.

Looking at this fine work as a whole—all three volumes—one is impressed by the great range of interest to be found within a group so relatively uniform that most of its members are included in a single sub-family. It is gratifying to have the information so competently and handsomely brought together.

LANDSBOROUGH THOMSON

Uganda in Black and White

By Hugh B. Cott. Pp. xxvi+232 (109 figures). (London: Macmillan and Co., Ltd., 1959.) 30*s*. net

AN unusual and delightful volume which seeks to fascinate the reader with the beauties of Uganda and its inhabitants by means of no less than 109 full-page drawings with brief explanations on the opposite pages. There is a short foreword by Sir Andrew Cohen, a former governor of the Territory, and a not much longer introduction by the author, and then we come to the pictures. Dr. Cott is interested in crocodiles, and the main reason for his sojourn in Uganda was to study the habitat of these unpleasant beasts. But he is also an artist with a keen eye for the country and the people. Much more can be done with drawings than is possible with photographs. The latter are doubtless factually correct, but there is something that drawings can give which the unselective photograph cannot. Dr. Cott is interested in the old Uganda, not in its Westernized modern developments. He does not pretend to have visited every single part of it, but he does give us pictures from many regions. There are pampas swamps and country scenes, dhows on Lake Victoria, a Muganda lady, and, of course, some crocodiles. A lovely picture of the Ripon Falls before they vanished when the new dam was built can be taken in conjunction with another two of the Murchison Falls. Then there are giraffe browsing and a serval cat, not to mention elephants, rhinoceros, and and an Ankole cow. Some of the characteristic carvings in hard wood of various animals, etc., are also illustrated, as well as the people themselves. Altogether a delightful volume which it is a pleasure to possess.

M. C. BURKITT

A Geography of Ghana

By E. A. Boateng. Pp. xvi+205+24 plates. (Cambridge: At the University Press, 1959.) 21*s*. net.

ALTHOUGH primarily intended for school examination candidates and first-year university students, this book deserves a wider public. Written by a Ghanian, who is now senior lecturer in the University College of his own country, for his own people, it reaches a high level in selection and presentation of material. An enclave surrounded by French-speaking territory, there has been some tendency for Ghana to be surveyed and studied in isolation, and it is useful to have summaries of local work in geology (with explanation of the special terminology), vegetation, soil and agriculture. A third of the book is devoted to a systematic treatment of the contrasted geographical regions. An excellent series of 41 photographs and 46 text figures and maps, all carefully prepared, completes a book of which Ghana may well be proud.

L. DUDLEY STAMP

THE CERN PROTON SYNCHROTRON

By J. B. ADAMS

In a recent article in *Nature*[1], in which a short review of the work of the laboratories of the European Organization for Nuclear Research (CERN) at Meyrin near Geneva, Switzerland, was given, it was mentioned that a 25-GeV. alternating gradient proton synchrotron was in an advanced stage of construction (Fig. 1). This accelerator has now been put into operation. Towards the end of November 1959, protons were accelerated up to 24 GeV. kinetic energy, and a few weeks later, after adjustments had been made to the shape of the magnetic field at field values above 12,000 gauss by means of pole-face windings, the maximum energy was increased to 28 GeV. The intensity of the accelerated beam of protons was measured as 10^{10} protons per pulse and there was no noticeable loss of particles during the whole acceleration period up to the maximum energy. The CERN proton synchrotron has thus fulfilled the expectations of its designers and the hopes of the twelve European countries that have supported the work for the past six years. It seems appropriate on this occasion to give a short account of this project together with a brief description of some of the design problems and preliminary measurements of the operating characteristics of this accelerator.

In June of 1952, at a conference in Copenhagen, the Interim Council of CERN decided to start an engineering design study of a 10-GeV. proton synchrotron that was to be the principal high-energy accelerator for nuclear physics research in Europe. The cost of this machine was considered to be so large in relation to other expenditures in physics research that no one European country felt justified in financing it alone. Hence several countries had combined their resources in order that physicists should have available in Europe the highest-energy accelerator that was thought feasible at that time. By July 1952 a design group of three people was set up with Dr. O. Dahl in charge, and in August this group, during a visit to Brookhaven on Long Island to see the cosmotron at first hand, learnt of a new idea for making cheaper and higher-energy machines. This idea was considered so attractive that in October 1952 the CERN Council was persuaded to drop the engineering study of a 10-GeV. proton synchrotron and instead to set up a theoretical study of the new principle. It seemed that a 30-GeV. machine might be built for the same cost as a 10-GeV. cosmotron type of machine. It is interesting to note that at this time, and quite unknown to the Western world, Russian scientists were planning a scaled-up version of the Berkeley bevatron for 10-GeV.

In December 1952 the Proton Synchrotron Group was formed to augment the original staff of three, and the members of this group, most of them honorary part-time members, remained in their own laboratories and institutes. Members of the theoretical section worked at the Atomic Energy Research Establishment, Harwell, and at the Universitetets Institut for Teoretisk Fysik, Copenhagen. The magnet studies were concentrated in the Laboratoire de Radio-électricité de l'Université, Paris. The radio-frequency problems were studied at the Institut für Physik, Max-Planck-Institut, Heidelberg. The radiation shielding problems at such high energies were worked out using cosmic ray data at the Physikalisches Institut der Universität, Freiburg-i.B., Germany, and the general engineering problems remained at the Chr. Michelsens Institutt, Bergen, Norway, where for six months two of the senior staff of the cosmotron, J. P. Blewett and M. H. Blewett, gave invaluable assistance with the general design problems of the new machine.

By October 1953 enough was known about the implications of the new idea to present a tentative design of an accelerator to the Council of CERN. In America, meantime, the Brookhaven group and another at the Massachusetts Institute of Technology, Boston, had been working on similar problems. At the end of October a conference was held at the Institute of Physics of the University of Geneva, to which were invited representatives of the American groups, the

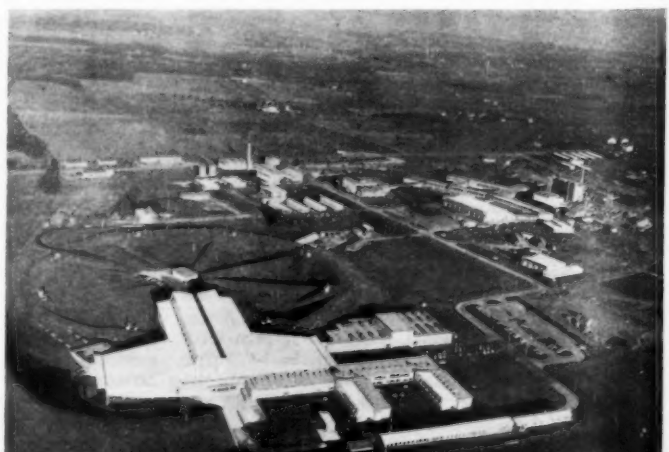

Fig. 1. Aerial view of the CERN proton synchrotron

Table 1

End of year	Main activities	Total staff*
1953	Preliminary studies	20
1954	Design of final machine	75
1955	Development of component parts	120
1956	Major contracts placed for components	150
1957	Manufacturing of components in firms	163
1958	Assembly of components at CERN	176
1959	Testing of components and commissioning of CPS	180

*This includes all staff directly connected with the design and construction of the machine

scientific members of the Council of CERN and other European scientists. The CERN Proton Synchrotron Group gave a series of lectures on its work of the previous ten months and presented a design for a 30-GeV. proton synchrotron using the new alternating gradient principle. It was found that the Brookhaven group had arrived independently at a very similar design.

Immediately after this conference the CERN Council fixed the energy of the machine at 25 GeV. and agreed that the members of the Proton Synchrotron Group should come together in Geneva, near which city the new European laboratory was to be sited. The State of Geneva and the University generously offered temporary laboratory accommodation, and by December 1953 most of the group had moved to Geneva with their families, and the task of designing the final machine started. Soon after this move Dr. O. Dahl resigned as director of the group, and the group suffered a further loss by the sudden death of Dr. F. Goward, who had been acting as deputy director. Despite these initial set-backs the group successfully established itself in Geneva. From the beginning of 1954 onwards staff was steadily recruited from all over Europe, and the group was built up as shown in Table 1.

The alternating gradient principle has been described many times. The original idea was published by E. D. Courant, M. S. Livingston and H. S. Snyder[2] and, quite unknown to these authors, was previously invented by N. Christofilos. In the conventional synchrotron the focusing of the circulating particles is achieved by arranging that the magnetic field which guides the particles around a fixed radius decreases slightly with radius. The amount of focusing achieved in this way is not very great, and consequently the amplitudes of the free oscillation of the particles are large and the dimensions of the magnet gap correspondingly large. Most of the cost in the original synchrotrons is in the magnet; for example, the Russian 10-GeV. synchrophasotron magnet, the radius of which is 30·5 m., contains 35,000 tons of steel and the magnet gap is 150 cm. wide and 40 cm. high. Although greater focusing can be obtained in the axial direction by increasing the gradient of the magnetic field, the criterion for radial stability is then violated. It is the great advantage of the alternating gradient principle that the focusing of the circulating particles can, in theory, be made as strong as one wishes and the amplitudes of oscillation of the particles as small as desired. This is achieved by alternating the sign of the gradient of the magnetic field many times around the circumference of the machine. The net result of this stronger focusing is to reduce greatly the weight of the magnet; for example, the CERN 25-GeV. proton synchrotron magnet has a useful aperture of 14 cm. × 7 cm. and contains only 3,400 tons of steel. It is 100 m. in radius, that is, three times the radius of the Russian machine and one-tenth the steel weight.

These attractive advantages are realized at the price of greatly increased accuracy in manufacturing and aligning the magnet of the synchrotron. Also, once the magnet is set up with the required precision, it must remain in place and, for a machine 200 m. in diameter, this presents some interesting foundation problems. The CERN proton synchrotron magnet is made up of 100 supposedly identical magnet units, each about 4·3 m. long. The magnetic field error between these units for the same energizing current should not exceed about one part per thousand, and the units should be set up with a precision of a few parts per million (0·3 mm. in 100 m. radius). The units are mounted on a free-floating monolith ring of concrete 200 m. in diameter and 2 m. × 2 m. in cross-section, and the machine is built in a subterranean annular tunnel in which the temperature is controlled to ± 1° C. As a further precaution, the concrete ring has steel pipes cast in it, and water is passed round the ring to prevent any part assuming a temperature different from the rest. The technology developed for the magnet construction and the foundations has been described in various CERN reports[3,4].

Another advantage of the alternating gradient principle is that the amplitude of momentum oscillations is very much smaller than in the conventional synchrotron. Since these momentum oscillations result in radial movements of the particles which have to be contained within the width of the magnet aperture, the alternating gradient synchrotron is again more economical in magnet aperture than the conventional synchrotron, in this case by a factor of about 60. Unfortunately, this improvement is also realized at the cost of imposing problems which, at the time of designing the CERN proton synchrotron, seemed formidable.

One restriction concerns the curious behaviour of the machine at an energy called the 'transition energy'. During the momentum oscillations in a synchrotron, particles with greater momentum than the mean value swing out to a radius greater than the mean radius. The revolution time of these particles depends on two factors which work in opposition. Because these particles have a greater momentum than the mean value, their velocity is greater than the mean velocity, and they take a shorter time to complete a revolution than the mean revolution time. On the other hand, since the radius at which these particles circulate is greater than the mean radius, they have a longer path to go round and this lengthens their revolution time. In an ordinary synchrotron, the 'radius term' is greater than the 'velocity term' and those particles with greater momentum than the mean value always take longer to go round than the mean particles. Due to the momentum compaction in an alternating gradient synchrotron, the radial displacement for a given momentum change is about a factor of 60 less than in a conventional synchrotron, with the result that at low energies, at the beginning of the acceleration cycle, the velocity term is larger than the radius term. However, as the energy increases and the particles approach the velocity of light, the velocity term decreases due to relativistic effects. Consequently, there comes a time in the acceleration cycle of the CERN proton synchrotron when the radius term equals the velocity term. The energy at this time is called the 'transition energy'.

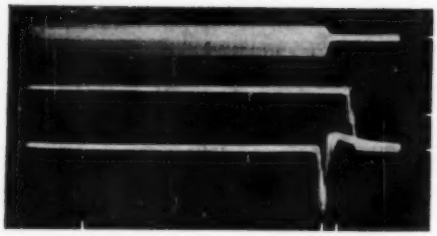

Fig. 2. Beam current versus time. Beam accelerated to about 24 GeV. with no loss

At this energy the frequency of the synchrotron oscillation goes to zero, phase stability is lost, and a rapid shift in the phase of the accelerating voltage has to be made so as to recapture after transition energy all the particles that have been accelerated up to that energy.

It is possible to design an alternating gradient machine so that the transition energy is higher than the maximum energy of the machine, but this can only be done by increasing the circumference of the machine by as much as 50 per cent with a consequent increase in cost. In fact, two new Russian alternating gradient machines have been designed in this way. However, in the case of the CERN proton synchrotron, it was calculated that the transition energy could be passed without loss of particles, and the operational results shown in Fig. 2 justify these calculations. It is possible that the Russian machines will now be modified and consequently will be capable of going to even higher energies.

The particles in a synchrotron circulate at a fixed mean radius, and in order to keep them in the centre of the vacuum chamber during the whole acceleration cycle the frequency of the accelerating voltage must track the steadily increasing magnetic field with high precision. The relative frequency error for a 1-cm. displacement of the mean radius of the circulating particles in the CERN proton synchrotron is given in Table 2.

Table 2

Kinetic energy of protons	$\Delta f/f$ for 1 cm. radial displacement
50 MeV. (injection)	$3{\cdot}5 \times 10^{-3}$
1 GeV.	$8{\cdot}3 \times 10^{-4}$
2 GeV.	$2{\cdot}7 \times 10^{-4}$
3 GeV.	$1{\cdot}2 \times 10^{-4}$
4 GeV.	$4{\cdot}5 \times 10^{-5}$
5 GeV. (transition)	0
10 GeV.	$7{\cdot}0 \times 10^{-5}$
25 GeV.	$7{\cdot}5 \times 10^{-5}$

It can be seen that another unfortunate effect of the transition energy is to impose impossible tolerances on the accelerating voltage frequency at and near that energy. This problem has been solved in the synchrotron in the following manner. From the injection energy of 50 MeV. to about 1 GeV. the accelerating voltage frequency is automatically determined from the magnetic field by an analogue computer having an accuracy of about one part in a thousand. At an energy very much less than 1 GeV., in the 100-MeV. region when the particles are firmly captured in phase-stable bunches, another frequency-controlled system is switched in supplementing the analogue computer. The second system uses pick-up electrodes to detect the phase of the bunches in the machine relative to the phase of the accelerating voltage frequency and, by means of a servo system, holds this phase difference constant at a prescribed value. In addition, the radial position of the circulating bunches of particles in the machine is detected by other pick-up electrodes and, by means of another servo system, the bunches are maintained in the centre of the vacuum chamber.

Apart from these specific problems peculiar to alternating gradient synchrotrons, there are general theoretical problems concerned with non-linear stability criteria which have been studied extensively. The CERN proton synchrotron is equipped with sextupole and octupole lenses to adjust non-linearities in the magnetic field of the machine. A complete description of the CERN proton synchrotron is in course of preparation[2,5,6].

Measurements so far carried out on the CERN proton synchrotron are necessarily preliminary and incomplete. It will take at least six months of measurement work before sufficient is known about the behaviour of the machine to exploit it as a working nuclear physics tool.

The intensity of the proton beam is surprisingly high at this early stage of operation. Protons are injected into the synchrotron at an energy of 50 MeV. from a proton linear accelerator the design of which closely follows that developed at the Lawrence Radiation Laboratory, Berkeley. One important difference, however, is that the CERN proton synchrotron linear accelerator contains magnetic quadrupole alternating gradient focusing in the drift tubes in place of the grid focusing originally used in the American machine. The CERN proton synchrotron linear accelerator has produced intensities up to 5 m.amp. peak although for the tests so far carried out with the synchrotron a collimated 1 m.amp. proton beam has been employed. A buncher and debuncher have been built for this linear accelerator, but neither has been used so far. With 1 m.amp. being injected into the synchrotron and single-turn injection, a capture efficiency of 20–25 per cent has been measured, corresponding to a circulating beam of 10^{10} protons per pulse. The pulse repetition rate at 25 GeV. is 20 per min.

The energy of the protons in the synchrotron has, so far, been calculated from the magnetic field at the time the beam disappears and the radius of the machine. The earliest operational runs were carried out without any of the correcting devices being employed, except for the self-powered pole face windings needed to correct eddy currents in the metal vacuum chamber at injection when the guiding magnetic field is only 140 gauss. The proton beam then disappeared at a magnetic field of about 12 k. gauss due to the number of free oscillations of the particles per revolution becoming an integer. As the magnet yoke becomes saturated, the focusing forces diminish slightly, and instead of the machine working in the stable region between the unstable resonance bands, the operating point is slowly forced into a resonance and the particles are lost to the walls of the vacuum chamber. In later runs the pole face windings were energized by programmed generators designed to

keep the focusing forces constant up to magnetic fields of more than 14,000 gauss and it was observed that all the proton beam then reached an energy of just a little more than 28 GeV., limited only by the peak magnetic field available in the CERN proton synchrotron.

An attempt has been made to measure the number of free oscillations per revolution in both the axial and radial directions (Q_V and Q_R) during the acceleration cycle. At injection, with the pulsed inflector voltages not energized and a 2-μsec. pulse of protons injected from the linear accelerator, the beam spirals inwards in radius due to the rising magnetic field for over one hundred microseconds, and the fractional Q-values can be observed in the two directions by pick-up electrodes sensitive to one or the other of the two directions of oscillation. For these measurements the beam is injected in such a way as to set up either axial or radial oscillations of the particles. During the acceleration cycle the Q-values were measured by pulsing the quadrupole correcting lenses at different times in the cycle and by variable amounts, and noting when the beam was lost. The nominal Q-values are both about 6·25, and if at a certain moment the quadrupole lenses are pulsed by an amount that shifts, say, the Q_R value to 6·0, the beam will be lost due to instability at a radial first resonance. Similarly, pulsing the lenses in the opposite direction by the same amount loses the beam due to instability at a radial second-order resonance at $Q_R = 6·5$. Apart from the shift of the Q-values when the magnet becomes saturated, it appears that they remain close to $Q_V = 6·3$, $Q_R = 6·2$ during most of the acceleration cycle. Using this same method, the unstable boundaries of the stable operating region, namely $Q_R = 6·0$, 6·5 and $Q_V =$ 6·0, 6·5, have been measured. So far, no higher-order resonances due to non-linear instabilities have been observed, although whether this is a tribute to the linearity of the machine or due to the crudeness of the measurements remains to be seen.

Measurements have been made of the closed orbit displacement at 20 points around the circumference of the machine, from which the closed orbit amplitude and shape have been computed. The closed orbit is that orbit around which all particles perform free oscillations. In a perfect machine without field-free sectors it would be a perfect circle in a plane. In an imperfect machine its shape and amplitude are due to the imperfections. At injection the peak-to-peak amplitude of the closed orbit in the radial direction is about 4 cm., and in the axial direction it is a few mm. Later on in the cycle the peak-to-peak amplitude diminishes in the radial direction to about 1 cm. and remains negligible in the axial direction. Since the vacuum chamber dimensions are 14 cm. in the radial direction and 7 cm. in the axial direction, there is therefore no danger of loss of beam due to magnet misalignments.

The transition energy, which seemed so formidable a barrier during the design stage, proved to be easily surmountable in practice. The precision of phase switching needed at transition for no noticeable loss of particles was found to be about ± 3 msec., or ± 36 gauss.

Both the computer and the beam control system for determining the frequency of the accelerating voltage have proved very satisfactory after minor adjustments. During the operational runs so far carried out the beam control system has been switched in about 1 msec. after injection and there seems to be no noticeable loss of particles during this switch-over. During the early acceleration studies the radial control servo acted on the amplitude of the accelerating voltage, which in principle is equally effective a means of controlling the radial position of the beam as varying the phase or frequency of the accelerating voltage. This arrangement was not successful, perhaps due to a certain amount of jitter in the phase-lock loop, and the system was modified so that the radial control servo acted on the phase of the accelerating voltage. This second method was completely successful and no particles were lost during acceleration. Preliminary measurements indicated that the beam was not moving more than 1 cm. from the centre of the vacuum chamber during the acceleration cycle. The beam control system depends for its operation on the presence of a bunched proton beam, and due to noise in the servo loops there is a certain minimum value for the circulating beam current below which the system no longer maintains control. It appears from early measurements that the system will work with about 10^8 protons per pulse.

Table 3

Accelerator	Max. energy (GeV.)	Mean intensity (particles per sec.)	Completion date
Brookhaven proton synchrotron (Cosmotron)	3	2×10^{10}	1952
Saclay proton synchrotron (Saturne)	3	10^{10}	1958
Princeton–Pennsylvania proton synchrotron	3	2×10^{11}*	1960
Berkeley proton synchrotron (Bevatron)	6	2×10^{10}	1954
Rutherford Laboratory proton synchrotron (Nimrod)	7	10^{11}*	1961/62
Russian A.G. proton synchrotron	7	$\sim 2 \times 10^{12}$*	1960
Russian proton synchrotron (Synchrophasotron)	10	$\sim 10^{9}$	1957
Australian proton synchrotron	10	10^{7}*	1962/63
Argonne zero gradient proton synchrotron	12·5	2×10^{11}*	1962
CERN proton synchrotron	28 25 6–10	2×10^{9} 3×10^{9} 10^{10}	1959
Brookhaven A.G. proton synchrotron	30	$\sim 3 \times 10^{12}$*	1960
Russian A.G. proton synchrotron	50	$\sim 10^{12}$*	1961/62

* Target figures.

A very important parameter of an accelerator is the mean intensity. Table 3 shows that at an energy of 6 GeV. the mean intensity of the CERN proton synchrotron is now nearly as high as that of the bevatron, and at 10 GeV. considerably higher than that of the Russian machine. It is hoped to increase the intensity of the CERN proton synchrotron by an order of magnitude by bringing into operation the buncher and debuncher of the linear accelerator and allowing more protons to be injected into the synchrotron. At 25 GeV. the yield of secondary particles from internal targets is considerably higher than at 6–10 GeV., and early measurements of secondary particle yields from the synchrotron indicate that the machine may be a strong competitor to the lower-energy high-intensity machines now being built from this point of view.

The significance of this accelerating machine can best be understood in relation to other proton synchrotrons. The CERN proton synchrotron accelerates protons to an energy which is about three times the energy of the largest accelerator now functioning, namely the Russian synchrophasotron

Table 4

	Maximum energy	Cost in million (Swiss francs)
CERN proton synchrotron	28 GeV.	120
Rutherford Laboratory proton synchrotron	7 GeV.	84
Saclay proton synchrotron	3 GeV.	53
Hamburg electron synchrotron	6 GeV.	60

at Dubna, and so, for a while, Europe possesses by far the largest accelerator in the world. In 1960 another machine of slightly higher energy (30 GeV.) will come into operation at Brookhaven in the United States, and in 1962 or thereabouts the Russians plan to bring into operation a machine twice as large as the CERN proton synchrotron (50 GeV.). The possession of the world's highest-energy accelerator is, and always has been, a transitory state, but the remarkable significance of this event is that for the first time for more than twenty years Europe can claim this possession. Since the War a major effort has been made in Europe to equip laboratories working in high-energy nuclear physics research with the necessary apparatus. The magnitude of this effort in terms of money is considerable, as can be seen in Table 4.

The cost of running these laboratories and building apparatus for the experiments is equally high, and this is a recurrent cost since new experimental apparatus is continuously being needed as the experiments develop. For example, the annual budget of CERN, which in addition to the CERN proton synchrotron also has a 600-MeV. synchro-cyclotron, is about 60 million Swiss francs per annum.

That Europe has made such an effort in this field of fundamental research has been due to the foresight of the physicists who have planned the laboratories and the sympathy of the national treasuries which have supplied the money.

[1] Adams, J. B., *Nature*, **184**, 944 (1959).

[2] Courant, E. D., Livingston, M. S., and Snyder, H. S., *Phys. Rev.*, **88**, 1190 (1952).

[3] Regenstreif, E., CERN 59-29. "The CERN Proton Synchrotron". Part 1. Ch. 1 : Basic Principles of Alternating Gradient Synchrotrons. Ch. 2 : Design of the CPS and Choice of Parameters. Ch. 3 : Magnet. Ch. 4 : The Radio Frequency Accelerating System.

[4] Adams, J. B., CERN 56-21. "The Design of the Foundations for the Magnet of the CERN Alternating Gradient Proton Synchrotron".

[5] Regenstreif, E., CERN 59-26. "Le Synchrotron à Protons du CERN, 2 ème partie. Ch. 5 : L'injection des particules" (English version to be published).

[6] Regenstreif, E., CERN. "The CERN Proton Synchrotron", Part 3 (in the press).

HUMAN ADAPTATION TO COLD

By Dr. LAURENCE IRVING

Arctic Health Research Center, U.S. Public Health Service, Anchorage, Alaska

THE people from whom we have gained our opinions about physiological reactions to cold have lived in clothing manufactured to common standards and in shelter of regulated warmth. Until recently physiologists have not been impressed by the significance of man's adaptability to cold. But we seem to forget that in every military campaign some soldiers have learned to perform well during prolonged exposure to cold which would have been unbearable in light clothing and poor shelter unless they had developed the adaptability that remains latent without training.

Recognizing this, Scholander *et al.* started expeditionary physiological studies of populations motivated and trained for exposure, including young Norwegians briefly trained in the cold[1] and three different ethnic groups ; Arctic Lapps[2], Australian Aborigines[3] and arctic Athabaskan Indians[4]. The results have demonstrated an unexpected range and variety of reaction to cold among people living in cold or chilly climates.

If development of adaptation to cold is associated in our minds with inability to obtain what we regard to be proper protection, we would disregard the many religious individuals and others that have elected to go in thin clothing with bare feet to practise humility and escape from the distraction caused by indulgence for bodily comfort.

The Alaskan members of the Wisdom, Knowledge, Faith, Love Fountain of the World commonly wear only a cotton robe and go with heads, hands and feet bare. They keep their clothing light out of regard for simplicity ; but it is their opinion that their garb is more comfortable than the designs of fashion. They avoid endangering themselves by their light clothing, for when the ground is too stony they put on shoes and they add further protection in severe cold weather.

Two young men, students at the University of Alaska, who have been members of the Fount at Venta, Alaska, for about two years, co-operated in measurements of their skin temperature. One of the students, *B*, stood for 64 min. in a room at an air temperature about 0° C., barefoot on a wood floor at − 1° C. to + 1° C., clad in shorts with a loose short-sleeved cotton robe. Towards the end he began to shiver slightly and at 42 min. the side of one big toe had cooled to 7·9° C., thereafter warming to 18·5° C. at 53 min. and cooling again to 15° C. at 64 min. At 17 min., when he remarked feeling both big toes warming, the recorded temperature on one toe had risen from a momentary low at 10·0° to 10·2° C. in the preceding minute and rose in the next minute to 10·4° C. At 34 min. the big toe had cooled again to 8·8° C., a change that he also reported as it began. At 42 min., when the toe was 7·9° C., it felt uncomfortable but not painful. 30 sec. later, when the toe had warmed to 8·6° C., he had already informed me of the warming. His body felt uncomfortably chilly, and he directed attention to sweating in the armpits which he said often accompanied reaction to chill.

The second student, *G*, stood in the cold room (air 1° C. to 2° C., floor − 2° C. to − 3° C.) for 34 min. His big toe cooled to 4·9° C. in 20 min. and to 4·6° C. in 34 min. At 20 min. his legs shivered in vigorous,

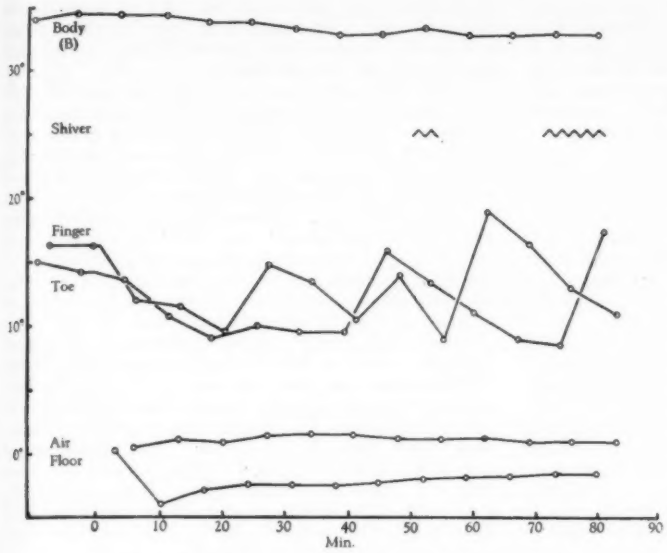

Fig. 1. Record of skin temperature in student *B*. Note the large swing of temperature in fingers and toes and the very slight shivering

intermittent bouts and he reported that his body felt warm and that his feet were not painfully cold. The test was not terminated by cold but owing to dizziness from standing.

On a second occasion, temperatures were recorded with the students sitting reading in the cold room, dressed as before. The record in Fig. 1 is for student *B*, and shows the average reading from two thermocouples on the back and one on the sternum (the three not differing more than 1·5° C.), one on the mid-finger pad and one on the big toe near the base of the nail. The tip of the middle toe held within 2° C. of the big toe. The outer side of the foot 2 cm. from the base of the little toe and the dorsum were about 10° C. warmer than the toes. Legs were intermediate between the temperatures of the body and feet.

The finger of student *B* began to warm and cool in long cycles after 20 min. (Fig. 1), his toes warmed at 40 min., and their warming at 60 min. was asynchronous with the warming of the finger. Student *G*, who shivered somewhat more but not vigorously, showed no clear-cut warming of the toes but a distinct warming of the finger. Although his toes were colder than 5° C. from time 65 to 100 min. they were not painful. The reactions to painful cold are usually so evident that it is unlikely that they could be deliberately suppressed and the students located and described their other sensations very accurately. Both students said that although they would not choose such conditions for study the cold did not interfere with their reading. Airman Henson, who assisted in the observations, and I were chilly in warm clothing as we moved in and out of the cold room.

A contrasting response was shown by the airman, who had been in Alaska for about two years. Sitting with bare head, hands and feet, and wearing only cotton fatigue jacket and trousers over shorts, about equivalent in insulation to the robes of the two students, his fingers and toes did not cool quite so low as those of the students (Fig. 2). He began shivering almost at once and continued in violent intermittent bouts which soon reached disagreeable intensity. After 8 min. his toes felt very uncomfortable and were very painful after 14 min. At 41 min. it was considered that his fortitude was not contributing further to physiology, and he reluctantly consented to terminate the test.

In spite of his shivering, which perhaps cooled him by ventilating his clothing as much as it contributed in metabolic heat, the airman's body skin cooled promptly. The two students had kept their bodies comfortably warm with but little shivering. As student *G*'s toes cooled to about 5° C. at 65 min., he remarked that they lost sensation and he could not detect a light touch with a pencil. The feet of all subjects were flushed and somewhat swollen, blanched on pressure and on release immediately reddened again. Spontaneous blanching of the feet was not observed, and judging by this criterion frost-bite was not imminent. After leaving the cold room the students rewarmed promptly with no pain; the airman took about 15 min. to regain comfortable warmth, with diminishing pain as recovery proceeded.

Although one of the students lost sensitivity in his toes when they cooled to about 5° C., otherwise both of them acutely observed their sensations of cold and warmth and located them with surprising accuracy, which surprised me and the airman. The students reported and located warming of even one toe by a fraction of a degree and accurately named the cessation of the warming phase of the cycles.

Student *B* pointed out that visible beads of sweat formed on his finger tips as they began to warm and showed me sweat beads on his warming toes after the tape covering the thermocouples was removed.

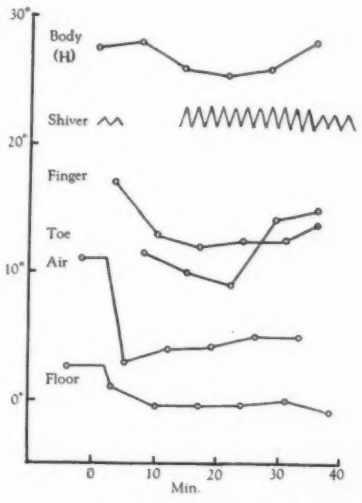

Fig. 2. Records of skin temperature in Airman Henson. Violent shivering with considerable fall of surface temperature

The airman also pointed out sweat on his still painfully cold toe as it warmed after the thermocouple was removed. Localized sweating thus appears to be connected with the vascular reaction which brings about warming of cold skin. It appears that local re-warming is associated with sweating. Sweating seems inconsistent with very cold skin; but the surprising combination may furnish a clue to the nervous component involved in peripheral regulation of temperature.

These adapted individuals appeared to have developed accurate appreciation for the temperature of their skin, keeping track of the changes at various locations at all temperatures down to about 6° C. They apparently deliberately utilize this conscious scanning of the thermal situation to avoid unsafe exposure. Eskimos also observe and care for the thermal situation in their faces and hands in extreme cold, and rarely experience frost-bite except through accident or when required by circumstances deliberately to tolerate the well-known sensations which warn of incipient frost-bite.

The freedom of the adapted men from pain caused by cold was associated with retention of adequate sensitivity and probably with improvement in the recognition of temperature of skin, its small changes and exact location. Keen appreciation of thermal conditions must be employed for the maintenance of skin to be safe at temperatures critically close to freezing, for, like hibernating animals, very cold tissues lack heat and the power for its production which buffer warm tissues against the fatal consequences of small depressions in temperature. I have remarked that sensitivity persists in the very cold feet of arctic birds and mammals which are still accurately guided by the sensations requisite for standing and movement[5]. Only sensitive feet can safely serve to economize on heat by cooling to nearly freezing, and it is obvious that insensitive tissues could perform no adaptive function.

It is also essential that any surface of an animal normally making contact with cold snow or ice should not become warm enough to cause melting or the skin or hairs would quickly freeze fast[6]. The students said that when they stepped from a warm room on to cold icy ground their feet became iced and picked up gravel, causing painful abrasions, although if icing did not occur their feet could withstand even − 20° C. for a time. Those who have hunted with dogs in cold snow will recall that the feet of some kinds become crippled by icing. The feet of healthy arctic animals do not commonly become iced as long as they are free to care for themselves.

After habitually wearing shoes, learning to walk with bare feet on rough ground involves some superficial hardening, but the process of learning to utilize the latent adaptability also involves improvement in operation of the senses which must direct the bare feet so that they are guided to avoid violent contacts with sharp or hard objects which no living tissue could withstand. In cold-adapted feet it is evident that the temperature causing cold pain is lowered, but sensitivity to temperature and the other senses necessary for the use of the feet must remain adequate for their effective operation.

These two students have deliberately practised exposure to cold in Alaska for only two years, but their exposure was less frequent and severe than among some of their people who worked out of doors. The airman appraised the practical importance of their adaptation by remarking on the advantageous mobility that would be gained by an infantry battalion trained to operate in such light clothing; but when I remarked that airmen would gain equally if relieved from some of the impediments of clothing and shelter he was less pleased with the idea.

It is apparent that human adaptability to cold is of practical importance when it is evoked by careful training motivated by consideration of benefit to be obtained from exposure. It is also apparent that adaptability to cold remains a latent faculty in urban populations.

Dr. Raymond J. Hock made instruments available from the Arctic Aeromedical Laboratory, and generously helped with preparations and part of the observations. His assistant, Airman First Class Harns C. Henson, of the Arctic Aeromedical Laboratory, gave skilled help throughout the experiments.

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COMMITTEE ON NATURAL RESOURCES IN SCOTLAND

By Dr. F. N. WOODWARD, C.B.E.
Arthur D. Little Research Institute, Inveresk, Midlothian

A COMMITTEE on Natural Resources in Scotland has been set up by the Scottish Council (Development and Industry) under the chairmanship of Mr. L. A. Elgood to examine the most suitable ways of developing and conserving Scottish primary resources. At the outset, two stages are envisaged: first, the setting-up of a fact-finding study group to provide information and, secondly, a subsequent conference of wider educational scope with emphasis on socio-economic problems.

The study group, which will meet at the Royal Society of Edinburgh during October 31–November 2, will comprise about fifty invited national and international experts in the various resource fields, who will discuss and review previously prepared papers designed to cover these problems in three phases, namely, individual resources already surveyed, the inter-relationship between them, and resource administration techniques and development.

The published proceedings of this fact-finding study group will not only make available to the public for the first time an up-to-date assessment of Scotland's primary resources, but also provide the background information for the subsequent more comprehensive conference which is intended for a larger, less technical audience, and would be designed to influence public opinion.

It is anticipated that the complete inquiry will cover a period of 3–4 years and inevitably lead to a change in the public's attitude towards problems of resources.

While it is not possible to anticipate the outcome, it is envisaged that the need for additional research institutions and for a permanent centre for information and for the co-ordination of the interests and efforts of those concerned with conservation and use of resources will emerge.

The setting up of the Committee on Natural Resources in Scotland is a logical if belated outcome of the United Nations Scientific Conference on the Conservation and Utilization of Resources which was held at the United Nations temporary headquarters at Lake Success in 1949. That Conference was unique among international conferences in that it provided a forum for more than six hundred scientists, conservationists and economists concerned with assessment, conservation and development of resources, drawn from fifty different countries. Their deliberations, in which the large British and Commonwealth delegation under the leadership of Sir Harold Hartley took an active part, in the presence of 350 observers resulted, among other things, in the production of seven volumes of "Proceedings" which are now recognized as the classic reference authority on world resources.

Among many suggestions emanating from the Conference was one to the effect that all countries should be regarded as under-developed, and that their known and potential primary resources should be examined afresh. This has been followed by resource surveys and conferences in various parts of the world. In the United Kingdom, however, there has been no comprehensive conference to follow the example set by the United Nations Conference. There are many reasons why such a conference would be difficult to organize, and even if it were, the outcome would be of debatable value ; but Scotland, on the other hand, presents a sufficiently compact region and has, at the same time, the diversity of resources to yield good results from such an inquiry. These resources are soil, water, minerals, fuel, fish and wild-life, forestry, and people of particularly interesting character.

A persistent problem in regard to the last of these is the continuous drainage of Scottish people through emigration. At present, about 40 per cent of Scottish graduates in science, and 60 per cent in engineering, leave to work elsewhere. While there are many examples of a flow in the reverse direction, the overall loss by emigration of trained men is too high and is a matter for serious concern.

There are other obvious resource problems awaiting solution in Scotland, and many more will doubtless be revealed as the inquiry develops.

For example, peat covers 1·7 million acres of land : if technical problems now under investigation by the Scottish Peat Committee are solved, a new industry could be established using an indigenous natural resource, with coincidental land reclamation for productive use. The conflict between agriculture, forestry and local authorities for land-use is being energetically tackled by the Scottish Departments and others : the attack on ancillary problems—such as the infestation by bracken of more than 0·5 million acres of land and the industrial use of agricultural crops and by-products—on the other hand, has been sporadic and frequently uninspired.

Although the demand for water is increasing rapidly, no single agency exists to survey and regulate water resources. There is a lack of hydrometric and underground water data and no standard technique for river flow gauging.

Also, although Scotland is very well surveyed geologically, very few geophysical surveys have been undertaken and no facilities exist for mineral beneficiation, research and development.

Due to historical trends, certain of the British natural resources agencies operate entirely within the Scottish regional context, whereas others have an overall United Kingdom interest. For example, fuel supply and forestry are dealt with on a United Kingdom basis, whereas agriculture is administered from a central Scottish headquarters ; water is not the concern of any particular agency.

Scotland's natural resource endowments, although significant, are relatively limited in number. Some of these, such as coal, oil-bearing shale, and water for hydro-electric power, have already been exploited, and others can, through research, form a source of wealth in the future.

In this respect, Scotland is handicapped in that its Government-supported resource laboratories, besides being small in number, are in imbalance. Though there are eleven concerned basically with the use of soil for agriculture, not one is solely devoted to forestry. The only other primary resource laboratories in Scotland are those dealing with fish, jute, peat, coal and nature conservancy ; none, for example, is available for undertaking research on mineral beneficiation, non-fish marine resources or chemurgy.

A good example of primary resource development is to be found in the new seaweed-based industry in Scotland which resulted from the co-operation between industry and an independent research organization specifically set up for the purpose.

Quite apart from the lead given by the United Nations Conference, it has been felt for some time that a new and integrated study of Scottish resources —including man—should be undertaken on the widest possible scale.

It is realized, of course, that such inquiry could result in recommendations which might affect certain present-day economic interests, although the ultimate result would be in the national interest.

The immediate use of peat for fuel, for example, might conceivably react to the detriment of future generations whose need for peat for water-storage purposes might be more vital. On the other hand, the locking of certain resources would not necessarily be a good thing, since unforeseeable changes, resulting from advances in scientific knowledge, could in the future make such action futile.

It is the hope of its promoters, however, that, among other things, the inquiry may be instrumental in preventing development of one resource from permanently damaging another, and thus avoid the chaos which has resulted in many parts of the world from haphazard and unco-ordinated development.

The Secretary of the Committee on Natural Resources in Scotland is Mr. H. M. Wilson, The Scottish Council (Development and Industry), Edinburgh.

OBITUARIES

Prof. Eric S. Horning

On November 14, 1959, British cancer research lost one of its prominent figures by the death of Dr. E. S. Horning, professor of experimental pathology in the University of London at the Chester Beatty Research Institute. Australian by birth, he served as a volunteer with the Imperial Forces during the First World War, and went to Oxford in 1920 to start his professional career in the honours school of comparative anatomy and zoology.

Having taken his degree, he went into research, first in Melbourne with Prof. Agar and later with A. Fischer in Berlin-Dahlem and E. V. Cowdry and A. Carrel in the United States. From this period stem numerous papers dealing with the behaviour of mitochondria and other cytological problems. The excellence of his early work was soon recognized. In 1932 he contributed by invitation an article on the enzymatic function of mitochondria to "Ergebnisse der Enzymforschung", and in 1941 he wrote in G. Bourne : "Cytology and Cell Physiology" the chapter on micro-incineration and the inorganic constituents of cells, a subject on which he was an authority.

Armed with a comprehensive knowledge of cytology and histology, and well versed in the methods of tissue culture, in 1933 he returned to England, the country he loved more than any other, where he spent the rest of his life but for the years of the Second World War, during which he served again with great distinction in the Armed Forces.

In 1933 Dr. Horning joined the staff of the Imperial Cancer Research Fund as a Beit Fellow ; when six years later the outbreak of war called him from the bench he had made his name as a cancer investigator. A series of brilliant papers had appeared in which Cramer and Horning recorded their original observations, shedding new light on the pathogenesis of the tumours of the breast, pituitary and thymus, and establishing the role of the adrenals in the development of these tumours.

In 1947 Dr. Horning accepted an invitation by Prof. A. Haddow to go to the Chester Beatty Research Institute as reader in experimental pathology. There he worked until the end, his scientific activities continuing unabated in spite of periods of indifferent health. Testimony to his persistent interest in the endocrinological aspects of cancer are the chapters in "Oestrogens and Neoplasia", his contribution to "Causation of Cancer" in the *British Medical Bulletin* 1958, and his papers on the experimental cancers of the prostate and the œstrogen-induced tumours of the kidney. Although from 1936 onward the role of hormones in neoplasia was the main theme of his endeavours, by his studies of the action of carcinogenic compounds on grafted tissues he made notable contributions to chemical carcinogenesis. Besides, his considerable experience with the pathology of the experimental and spontaneous tumours of rodents made him an invaluable collaborator in many projects of the Chester Beatty Research Institute. *Inter alia*, he described with Boyland the tumours induced by nitrogen mustards in mice, and with Alexander the reaction of the subcutaneous tissue of the rat to implanted plastic films.

Anybody who had the privilege to visit Dr. Horning in his laboratory and to look at some of his slides could only admire the beauty of his histological preparations, and was no longer astonished by the excellence of the photomicrographs which adorn his papers. The high quality of the material on which Dr. Horning's results were based and the elegance of his techniques rather than ingenuity of speculation were the basis of the high esteem he enjoyed among his colleagues at home and abroad. But, above all, few men had his gift for friendship and a heart so warm and generous. Only those who have worked with him know how easy he made life for his collaborators and how much he did unselfishly to further the work of the Institute. For his human and scientific qualities the memory of Eric Horning will be cherished in many lands.

F. Bielschowsky

Mr. W. E. Dick

With the sudden death of William E. Dick at the early age of forty-five, scientific journalism has lost one of the greatest exponents of this now rapidly expanding and increasingly important field—a field which shows signs of becoming to-day almost as important to the scientist, as a means of keeping him informed of developments in other fields as well as his own, as to the intelligent layman who wishes to learn about scientific and technological progress. He was successively editor of *Discovery* (1945–56), *British Chemical Engineering* (1956–58), and *Chemistry and Industry*, the journal of the Society of Chemistry and Industry. Prior to that he had held posts on the *Grantham Journal* (1941) and the *South Western Star*, which he joined in 1942. For a brief period he then worked as assistant editor to *Chemical Age*, before joining *Discovery* in a full-time capacity in September 1944.

William Dick was born at Walthamstow on July 12, 1914, and was educated at King's School, Wimbledon, where he took a State scholarship at the age of fifteen to the Imperial College of Science and Technology to read biology. Although he left the Imperial College before his degree was completed, his training was not purely journalistic, for he later became a qualified scientist, taking an external B.Sc. degree at the Chelsea Polytechnic in 1942. He was also elected a Fellow of the Linnean Society.

During the War he served with the Auxiliary Fire Service during the first months, and then at the British Expeditionary Force, Royal Army Service Corps Headquarters in France before being evacuated when France surrendered. Then he transferred to one of the camouflage units of the Royal Engineers at Farnham. He entered journalism in August 1941, after being invalided out from the Army.

When Bill Dick became editor of the newly revived *Discovery*, science writing was still, as I was made only too well aware on numerous occasions, regarded as a 'bastard art', more often than not despised by the scientist and badly handled by the Press. By setting a standard of journalistic and scientific reporting that raised *Discovery* from being a relatively unknown journal to one that had a readership throughout the world, and was renowned and highly

regarded as a scientific paper, Dick showed and taught others that science writing could be a valued and respected branch of science. In the process he also not merely set a new standard for other people to follow, but also helped to give invaluable advice and training to many new-comers venturing into this field. Besides his activities as editor for *Discovery*, Dick also wrote many articles, one of the best known of which was "Science and the Press", which was written in 1954 for the journal *Impact*. Here he set out many of the problems he had encountered and the ideals in which he believed. He also wrote, or contributed to, a number of books as, for example, "Science and the Welfare of Mankind", written in conjunction with I. B. N. Evans, published by Simpkin Marshall in 1946, and "The Story of Energy", published in 1951 for the Bureau of Current Affairs. In 1957, Butterworths Scientific Publications brought out his "Atomic Energy in Agriculture".

Dick's interests, indeed, were catholic in the extreme, every field of science intrigued and on occasion excited him, although professionally by qualification he was a biologist. The latter fact explains perhaps to some degree his immense interest in flowering plants and the joy and enthusiasm which he brought to his gardening.

Despite his many achievements, William Dick suffered for twenty years from a long series of illnesses of increasing severity. The debt owed him by scientific journalism is immense, and his early passing is an occasion of great sadness. Personally, also, he will be missed as one of the kindest and most generous of people, especially in times of trouble.

DEREK WRAGGE MORLEY

IT is impossible to conceive of any scientist, certainly of any editor or journalist, who was not shocked by the news of Bill Dick's sudden death or who will not now miss his entertaining chatter and stimulating pronouncements on science, especially on the exposition of science.

Although he was initially a reporting journalist and eventually an editor, he was never satisfied merely to sit down and rewrite into more readable form scientific reports and research publications which came to hand. He really believed that the good editor wears out the soles of his shoes rather than the seat of his pants. He went after news personally and wrote it up personally. For this reason alone, it is true that as Mr. Wragge Morley writes: "*Discovery* [metamorphosed] from being a relatively unknown journal to one that had a readership throughout the world, and was renowned and highly regarded as a scientific paper". Though *Discovery* still maintains this excellent standard, I am sure the present editor would be the first to admit that this happy editorial evolution was originally inspired by Bill Dick.

Dick's remarkable achievements and his engaging, though somewhat naïve, personality did not pass unnoticed, especially among his journalistic and editorial colleagues. For example, 1956 saw the tenth anniversary of the new *Discovery* which coincided with the tenth anniversary of Bill Dick's editorship. To mark this double event, a sherry party was held to which only editors and science writers were invited. It was significant that everybody who had been invited attended to pay tribute to Dick and *Discovery*.

Bill had a warm heart and a ready tongue. He had a real gift for nosing out news. His sincerity could never be challenged, for if he admired a person or his achievements he was lavish with praise; but woe betide anybody who, in his opinion, was not playing the game. You always knew how you stood with Bill.

It is a tragedy that science and especially the exposition of science (mainly through popular publications) has now to suffer the loss of this remarkable man; for science still suffers from a dearth of good writers, in spite of the fact that, as Mr. Wragge Morley says: "Science writing [is] a valued and respected branch of science".

The presentation of scientific advancements and achievements in an understandable form has now become an essential branch of science itself. Research cannot go on indefinitely behind closed doors; there must eventually be a fearless exposition and interpretation of the truths it unfolds. Bill Dick believed this and worked selflessly and passionately to this end.

L. J. F. BRIMBLE

Dr. H. P. Wilkins

HUGH PERCIVAL WILKINS, the distinguished selenographer, died at his home at Bexleyheath, in Kent, on January 23.

Wilkins was never a professional astronomer. He was born and educated in Carmarthen, and after serving in the Army during the First World War he became an engineer. His main interest lay, however, in astronomy. Though he made useful planetary observations from time to time, he concentrated almost entirely upon the Moon, and by 1924 had completed a lunar map 60 in. in diameter. Eight years later he commenced work upon an even larger chart, to a scale of 300 in. to the Moon's diameter. A prodigious amount of work went into this project; except during occasional periods of ill-health, Wilkins was nearly always busy at his telescope whenever the sky was clear and the Moon visible. The 300-in. map was published in 1951, and he then undertook a further revision, which appeared in 1954. Yet another revision was planned, though unfortunately he did not live to complete it.

After his marriage, Wilkins moved from Wales to Kent, and set up a 12½-in. reflector, later replaced by a 15½-in. instrument. It was with this equipment that he carried out most of his work, though he also made numerous observations with very large instruments in both Europe and the United States. He was a regular contributor to many scientific periodicals, and held the position of director of the Lunar Section of the British Astronomical Association from 1946 until his resignation ten years later. In 1941 he gave up practical engineering, and joined the Ministry of Supply, retiring only at the end of 1959 with the intention of spending the last part of his life in astronomical work.

Wilkins was well known as a lecturer on astronomy; he made frequent broadcasts on both sound radio and television, and was the author of seven books, the last of which was completed only a few days before his death. In 1955 the University of Barcelona conferred on him an honorary Ph.D. degree in recognition of his work for selenography.

Wilkins was above all a kindly man; he was unfailingly courteous, and could never understand those who were not. His enthusiasm for astronomy was inspiring, and he was always ready to help others. A deep sense of personal loss will be felt by his many friends all over the world.

PATRICK MOORE

NEWS and VIEWS

Chemical Engineering at Swansea : Prof. E. S. Sellers

Prof. E. S. Sellers resigned his post as head of the Department of Chemical Engineering, University College of Swansea, on January 31, to join the British Petroleum Co. as manager of the Petroleum Division at the Sunbury Research Centre. When in 1955 Prof. Sellers went to Swansea from the Department of Chemical Engineering, University of Cambridge, he faced the task of building a new department in a College that planned unusually rapid extension to its facilities for education in applied science. He leaves a department of chemical engineering with a well-established teaching programme that makes provision for the admission of some thirty honours students annually and the expectation of expansion to an entry of fifty students when new accommodation becomes available during the next five years. A special feature of the course for chemical engineers in Swansea has been the more than usual involvement of local industry. A considerable part of the practical work for undergraduates has been carried out on industrial plant rather than on laboratory equipment in the Department. This has been made possible by the excellent relations that the Department of Chemical Engineering has established with industry. During his period in Swansea, Prof. Sellers has supervised research on the flow of non-Newtonian liquids and the control of continuously operating process plants. In 1957 he was awarded the Moulton Medal of the Institute of Chemical Engineers for work (with Dr. D. R. Augood) on the distillation of hydrogen. He has served the Institution of Chemical Engineers as a member of the Council and on the Board of Examiners. He has been a member of several advisory committees of the Admiralty and the Ministry of Supply.

Prof. J. F. Richardson

Prof. J. F. Richardson, who succeeds Prof. E. S. Sellers at Swansea, graduated at the Imperial College of Science and Technology in 1941. After six years of postgraduate research with Sir Alfred Egerton, he was appointed lecturer and later senior lecturer at the College. In 1958 he resigned his university appointment to join the Development Division of Messrs. A. Boake Roberts and Co., Ltd., as senior chemical engineer. Prof. Richardson has served the Institution of Chemical Engineers for four years as a member of the Board of Examiners, as honorary librarian since 1954, and as a member of the Nominations Committee, the Careers Advisory Committee and the Advisory Panel on student membership. His publications cover a wide range and include a text-book on chemical engineering written jointly with Prof. J. M. Coulson. During 1941–47 his work was largely concerned with laboratory and large-scale studies on fire prevention and extinction. More recent research by Prof. Richardson has related to the physical properties of two-phase systems.

Royal Naval Scientific Service : Mr. J. Buckingham, C.B.

Mr. John Buckingham, who recently retired from the Royal Naval Scientific Service, where he held the post of director of research programmes and planning, joined that Department as a technical assistant in the Board of Invention and Research in 1917 and made naval science his career. During the years between the Wars he played an important part in the development of what was ultimately to become the Royal Naval Scientific Service. He was the assistant and confidant of the first director of scientific research, Dr. (later Sir) Frank Smith, and of his successors. The last of these, Mr. (later Sir) Charles Wright, selected him in 1936 as his deputy, a post he filled for ten years. In 1946 he was appointed the first director of research programmes and planning, with special responsibility for the management of peace-time research and development expenditure. Successive controllers of the Navy have spoken warmly of the skill with which these duties were carried out. He served on various Admiralty committees and represented the Admiralty on outside committees, always with distinction. His valuable advice was sought officially and unofficially by high and low on almost any matter which was 'tricky', and what he did behind the scenes often determined the success of actions in which officially he took no part. His many important works were recognized in 1953 by the award of the C.B.

Dr. W. E. Pretty

With the retirement of Mr. Buckingham, the Department of Research Programmes and Planning has been absorbed into a new Department of Research and Development Services; Dr. W. E. Pretty has been appointed to be its first director. As a Royal Scholar, Dr. Pretty was awarded the A.R.C.S. and the Governors' Prize in physics at the Imperial College of Science and Technology in 1925, and in the same year took his B.Sc. (first-class honours), London. For the next six years his time was spent between teaching and research at the College under Prof. A. Fowler. His researches in spectroscopy gained him his Ph.D. degree. In 1931 he joined the Science Museum as assistant keeper in charge of the optics and the astronomy collections. He served as secretary to the Advisory Council of the Museum and was much concerned with the successful introduction of a new type of 'special exhibition' showing really up-to-date science and technology in a particular field. In 1939 he was seconded to the Admiralty Department of Scientific Research and at the end of the War accepted an invitation for permanent transfer to the newly formed Royal Naval Scientific Service. He was promoted to the rank of deputy chief scientific officer and appointed director of research programmes and planning in 1948.

Toxic Chemicals in Agriculture

The Minister of Agriculture, Fisheries and Food, with the Minister for Science, the Secretary of State for Scotland and the Minister of Health, have appointed the following Research Study Group to consider this subject: Prof. H. G. Sanders, chief scientific adviser (agriculture), Ministry of Agriculture, Fisheries and Food (*chairman*); Dr. H. R. Barnell, chief scientific adviser (food), Ministry of

Agriculture, Fisheries and Food; Dr. J. M. Barnes, director, Toxicology Research Unit, Medical Research Council; Prof. A. R. Clapham, professor of botany, University of Sheffield; Dr. R. A. E. Galley, director, Tropical Products Institute, Colonial Office (officer-in-charge, Colonial Pesticides Research); Mr. C. O. Harvey, Laboratory of the Government Chemist (Department of Scientific and Industrial Research); Dr. Donald Hunter (physician to the London Hospital and part-time physician-in-charge, Department of Research in Industrial Medicine, London Hospital); Mr. W. C. Moore, director, Plant Pathology Laboratory, Ministry of Agriculture, Fisheries and Food; Prof. W. L. M. Perry, professor of materia medica, University of Edinburgh; Mr. G. G. Samuel, scientific staff (headquarters), Agricultural Research Council. The terms of reference for the Group are: "To study the need for further research into the effects of the use of toxic chemicals in agriculture and food storage, and to make recommendations". The Group is independent of the interdepartmental Advisory Committee on Poisonous Substances used in Agriculture and Food Storage, which will continue.

Corrosion Science Society

THE Corrosion Science Society has been founded with the following immediate aims: (1) to promote the advance of corrosion science and its application to the solution of practical problems; (2) to organize meetings—personal, local, national and international—of scientifically qualified persons interested in all fields of corrosion and corrosion-protection research and practice, for the discussion of current work; (3) to co-operate with all other professional individuals, societies and institutes, British and foreign, with interests in the corrosion field. The first meeting will be held during April 4–5 at the Battersea College of Technology, London. Stress-corrosion, cracking, the corrosion and protection of aluminium, cathodic protection, electrode processes and high-temperature corrosion and oxidation will be among subjects to be discussed on the basis of a series of talks by workers at present active in these fields, including C. Edeleanu, J. G. Hines, T. P. Hoar, J. E. O. Mayne, N. F. Mott, E. C. Potter and L. L. Shreir. Those interested should write to either Dr. T. P. Hoar, Department of Metallurgy, Pembroke Street, Cambridge, or Dr. L. L. Shreir, Battersea College of Technology, London, S.W.11.

Research in the German Federal Republic

ON behalf of the Federal Republic, the German Embassy in London publishes quarterly an attractive journal, *Germany*. A recent issue was devoted to fundamental research and its application (**4**, No. 12; 1959). The main articles deal with plastics and their place in the German economy together with accounts of the work being carried out in the different plastic research institutes. Prof. Curt Hoffmann, of the Institute of Oceanography, Kiel, is the author of an essay on marine production biology, and Prof. K. O. Kiepenheuer, of Freiburg, describes solar research in Germany. To inaugurate a series of portraits of German Nobel Prize winners, there is an illustrated account of the life and work of Prof. Otto Kahn. The journal also contains articles describing various aspects of cultural life in Germany, the most interesting portraying celebrations in connexion with the Schiller bicentenary in West Germany. The annual subscription to the journal is D.M. 20.

The Burma Research Society

DURING 1910 a small group of Burma residents, mostly Civil servants with varied interests as amateurs in the natural history, archæology, history and literature of the country, established a society to serve as a forum for their discussions and a *Journal* for the publication of their findings. The creation of the University of Rangoon ten years later brought many well-qualified recruits to the Society and the University gave it a permanent home. The thirty-one volumes of the *Journal* published between 1910 and 1941 include many original papers of first-class importance, but everything came to an end with the Japanese occupation. All records and stocks of publications went on the bonfire of the University Library and very few complete sets of the *Journal* seem to be in existence. The Society started up again in 1948, and it was a happy thought of its 700 members, headed by the president, the Hon. U Chit Thoung, Minister of Culture, to mark the fiftieth anniversary by holding a six-day conference during December 28, 1959–January 2, 1960. Twenty-one papers were read and a further fourteen contributed to be published in a single volume with the conference proceedings. Some fifteen overseas visitors were guests of the Burma Government and were afterwards taken to Pagan, ancient capital of Burma, incredibly rich in archæological and historical treasures, still in course of study by Prof. G. H. Luce and others. At the conference, Britain was represented by Dudley Stamp (professor of geology and geography in the University of Rangoon, 1923–26). To further mark the occasion, the Society is reprinting the more important papers of its pre-war *Journal*. There are to be three volumes—respectively History and Literature (published), Economic and Social, and Science, obtainable from the Society, c/o University Library, Rangoon, at kyats 20 (30*s*.) each. The Science volume includes eight geological papers, and a number on earthworms, tapeworms, algae and agricultural pests. A complete index to the *Journal* is also to be published.

Scientific Societies in the United States

THE U.S. Office of Science Information Service recently distributed a questionnaire to more than two hundred national scientific societies (*Scientific Information News*, **1**, No. 4; Aug.–Sept. 1959). The questionnaire is part of a study designed to provide objective information about the human and financial resources of scientific societies and their publications. Data requested by the questionnaire include: (1) total membership and distribution of members among various membership categories; (2) titles, frequency, and subscription rates of society publications; (3) sources of income, including subscriptions and endowments. This study of scientific societies is the first step in a wide-ranging programme designed to provide a clearer picture of scientific communication in the United States. The results of two other National Science Foundation studies—one of the policies, practices and costs of professional scientific journals and the other of scientific man-power data gathered by the National Register of Scientific and Technical Personnel—will be correlated with the scientific society study to help the Office of Science Information Service carry out more effectively its task of fostering co-operation and co-ordination among scientific information sources.

Darwin's "Journal"

In his "Autobiography", Darwin referred to a "little diary, which I have always kept", in which he recorded the work on which he was engaged, the time which he took in completing each of his researches, the books in which they were described, and his movements from place to place. The document itself was headed "Journal". Francis Darwin also referred to his father's "Diary or Pocket-Book" as having been of great help to him in writing and compiling "Life and Letters". He added that "it was unfortunately written with great brevity, the history of a year being compressed into a page or less, and contains little more than the dates of the principal events of his life, together with entries as to his work, and as to the duration of his more serious illnesses". Some important quotations have been published from the "Journal", such as the famous entry under the date 1837: "In July opened first notebook on 'transmutation of species'. Had been greatly struck from about month of previous March on character of South American fossils, and species on Galapagos Archipelago. These facts origin (especially latter) of all my views". Edited by Sir Gavin de Beer, the "Journal" has now been published as a Bulletin in the Historical Series of the British Museum (Natural History) (2; No. 1). Students of evolution will be grateful to Sir Charles Darwin and the Syndics of the Cambridge University Library for granting permission for this rich chronological story to be published.

Preserving the Amenities of Great Britain

An interesting example of the zealous way the Council for the Preservation of Rural England safeguards the amenities of Britain is revealed in its report for 1958–59. Its Central Panel Committee has recently considered the implications arising from the fact that the output of pressed Oxford clay bricks is now approaching 50 per cent of the entire production of all bricks in England, Wales and Scotland. Enormous quantities of these bricks are in general use within an area at least as far as 160 miles distant from the main producing area in Bedfordshire. As the appearance of new buildings throughout this area is linked with the type of brick available, the Committee felt that the manufacture of a reasonably wide variety was a matter for which the industry had great responsibility. These views were expressed in a letter to the Pressed Brick Manufacturers' Association. In reply, the Committee was informed that several new varieties are now on the market, and it is hoped that this policy will be promoted by the Association. The recent production of an attractive grey facing brick by the London Brick Co., suitable for use in stone districts such as north Bedfordshire, and adjacent parts of Northamptonshire, is a useful addition to the varieties now available.

Nature Protection in U.S.S.R.

Mr. G. Aliev, of the Academy of Sciences of the Soviet Republic of Azerbaijan, has described the text of a new law for the protection of Nature which was passed in the Republic in June 1959 (International Union for Conservation of Nature and Natural Resources, Bull. 8; Oct. 1959). The Commission for the Protection of Nature of the Academy of Sciences played a leading part in preparing and supporting this law. The Act provides for the conservation of the resources of the inanimate world and of living species, as well as the constitution of nature reserves and partial reserves. The same Act specifically mentions some interdicts: prohibits all economic activity within the reserves which would be contrary to their objectives; all interference with the places and objects preserved; all sale and purchase of reserved territories; all breaches of the hunting and fishing regulations; all uncontrolled introduction of exotic species; as well as undertakings which might result in air or water pollution, or begin or aggravate the process of erosion, the last being a source of grave problems in Azerbaijan. Any violation of the Act is considered a breach of Article 138 of the national constitution, which aims at "protecting and strengthening the sacred and inviolable foundation of the Soviet regime: public and socialist property". The Council of Ministers of the Azerbaijan S.S.R. and certain other Government departments have been charged with a number of duties relating to the protection and restoration of natural resources as well as measures against pollution and erosion; scientific preparation of natural resources of development schemes, recommendations, as well as the spreading of the principles and aims of conservation of Nature.

Liquified Petroleum Gases

Liquified petroleum gases are petroleum hydrocarbons which are gaseous at normal temperatures and liquified by pressures of a few atmospheres; they are thus easily stored and transported as liquid in relatively light pressure containers. 'L.P.G.', as they are known, may be derived from wet natural gas containing propane, butane and higher hydrocarbons; refinery distillation, whence propane and butane are obtained from crude oil by pressure distillation; cracking and reforming refinery processes. In a paper by R. F. Horner, P. C. Jarvis and A. G. Turner, at a symposium on the Uses of Liquified Petroleum Gases at the Institute of Fuel during December 1959, are described composition and properties of 'L.P.G.'; historical market development; applications; supply and distribution; future uses in the United Kingdom. Among other advantages is facility of handling and burning; precautionary measures must be taken in design of plant, because of their higher vapour pressure than ordinary liquid fuels. Combustion characteristics of 'L.P.G.' are high calorific value, specific gravity and high volumetric proportion of air required for combustion compared with coal gas; low flame velocity and narrow limits of inflammability compared with coal gas, hydrogen or acetylene. In a complementary paper by J. P. Liotier at this symposium is an account of "Uses of 'L.P.G.' in Industry in France with Particular Reference to the Metallurgical and Ceramics Industries", following developments for commercializing propane in French industrial markets, originally sponsored by L'Utilisation Rationelle des Gax.

Progress in Microchemistry

The *Microchemical Journal*, **3**, 3 (August 1959), contains a collection of review articles on various aspects of microchemistry which might be considered to have a wider appeal than the normal quarterly volume of this journal. The collection, which is generally of a high standard, suffers from a great variation of treatment by the twelve authors who contribute the articles. As an example, the section dealing with "Progress in Elemental Quantitative

Organic Analysis 1958" is very much to the point and gives good coverage to the work in this very important field, while the article dealing with "Progress in Qualitative Inorganic Analysis 1958" is written as a piece of special pleading for the replacement of classical techniques by others recommended by the author without sufficient explanation for his choice. The bibliography covers a wide range and has more references to European work than is sometimes found in American publications. This is probably a reflexion of the world-wide interest in microchemistry. There appears to be no reference in any of the sections to the determination of traces of residual pesticides in animal and plant tissues. This subject, which has a literature as extensive as the whole of the volume under review, would have added to the general value of the collection and could have provided material for discussion of the determination of sub-microgram quantities of organic compounds. The short section on equipment refers exclusively to American instruments. Subjects covered are, microscopy, fractionation and inorganic, organic and biochemical analysis. On the whole this is a useful collection of papers.

Russian Review of Biology

THE Institute of Biology, in collaboration with the Department of Scientific and Industrial Research, is to publish an English translation of the *Russian Review of Biology* (Oliver and Boyd, Ltd. £9 for nine numbers in all for 1959 and 1960, and £6 10*s*. per annum for six numbers thereafter). The Russian journal has been running for many years, and contains summaries, each dealing with progress in a specific topic of biological research. The first translated number starts with a polemical discussion of a work by Lenin in relation to Soviet materialist biology. This is followed by review articles on two enzymes (polynucleotide phosphorylase and xanthine oxidase), the use of enzymes in biological investigation, erythrocyte sedimentation and, finally, the immunological reaction in embryos and new-born animals. There are extensive bibliographies, which, incidentally, indicate the familiarity of Russian biologists with research throughout the world. This new translation will help to acquaint more English-speaking workers with the biological research going on in Russia. Under 'current events' there is an appreciative account of a visit by Kh. S. Koshtoyants to some of the biology departments at Cambridge.

Sarawak Museum

THE *Sarawak Museum Journal*, Vol. 8, of June 1958 is edited by Mr. Tom Harrisson, Government ethnologist and curator of the Sarawak Museum, and includes some characteristic forthright editorial comments. The volume is divided into five parts—the past, the present, some recent Borneo writing reviewed, Borneo plants and animals, and climate. Although the majority of the articles are of interest chiefly to those who live in Borneo, others, such as a paper on pollen from the South China Sea by Dr. F. R. Van Veen, are of more general application.

Bronze Figures from Nigeria

AN illustrated article on some bronze figures from Ita Yemoo, Ife, Nigeria, by Frank Willett, the archæologist of the Department of Antiquities, appeared in the November 1959 issue of *Man*. The finds were unearthed by chance, and luckily Bernard Fagg, the director of antiquities, happened to be in the vicinity. As a result, all particulars of their occurrence, etc., were collected, and the finds themselves carefully preserved. Like the pottery figures discovered some time earlier, they are of great interest, though, perhaps, not so beautiful. An interesting fact is that five of the bronze heads are gagged, and they probably represent victims for sacrifice in view of the sherds of a ritual pot found nearby. Doubtless all these various art discoveries in Nigeria will be published in book form in due course.

Mathematics and Children

AN article by Z. P. Dienes, lecturer in mathematics in the University of Leicester, in *Educational Research* shows that there are ways in which mathematical concepts can be caused to develop in children so that the techniques they learn are preceded by an understanding of the corresponding mathematical structures (*Educat. Res.*, 2, No. 1; Nov. 1959). Dienes's scheme has not yet been tried out under actual school conditions, but it is possible to state some qualitative results derived from trials in a number of schools. Schemes of individual mathematical discovery can be worked in large unstreamed classes throughout junior schools; a large majority of normal children can understand the complex workings of the four rules of arithmetic in the decimal and other systems; normal 10-year-old children can learn the use of brackets, the properties of the square, the solution of linear and quadratic equations and the factorizing of quadratic functions, if approached constructively.

It is possible to give children leaving junior school a solid body of practical experiences, impossible to obtain from real-life situations, on which an extensive secondary school curriculum can be based. There are almost limitless possibilities for enlarging the junior school syllabus, by including such topics as theory of groups, usually reserved for university honours courses. There is sufficient evidence to suggest that mathematics can be introduced to a larger section of the child population than had hitherto been thought practicable or possible. This is done by co-ordinating the teacher's work with the natural process of concept formation in the child. It is a challenge to the teaching profession to devise ways in which this much larger body of children can be drawn into the mathematical workshop. By doing so, a large potential of future mathematicians, scientists, and technicians would be created, whose practical bias is likely to make them extremely useful members of an increasingly technological society.

Preventing Evaporation from Reservoirs

VAST quantities of water evaporate from storages located almost everywhere in Australia. Much of the pastoral land lies in regions where evaporation from a free water surface exceeds 6 ft. a year, and annual losses of 8 ft. are not uncommon inland. The Mansfield process, devised by Mr. W. W. Mansfield of the Division of Physical Chemistry of the Commonwealth Scientific and Industrial Research Organization (Australia), has provided pastoralists and farmers with a simple method of cutting these enormous losses by at least a quarter. The process involves spreading a very thin film of hexadeconal (a pure form of cetyl alcohol) over the surface of stock tanks and small farm dams. The film is continuously

replenished as required from beads of hexadeconal housed in a small raft with gauze windows. Because of its enormous potential significance, details of the Mansfield process were released at an early stage in its development. This has allowed more experience to be accumulated under different conditions throughout Australia, and widespread use on thousands of dams has confirmed its potential value. However, further use has emphasized that good results are not obtained unless the raft used meets the Commonwealth Scientific and Industrial Research Organization requirements. The condition of the raft must be checked periodically. A recent article discusses some of these practical points, and describes how the few unforeseen difficulties that have cropped up can be overcome (*Rural Research in C.S.I.R.O.*, No. 28; June 1959).

Research in the Hat and Feltmaking Industries

The twelfth annual report of the Director of Research, British Hat and Allied Feltmakers Research Association, covering the year ended August 1959, stresses the addition to the research programme of a study of the shock-absorbing properties of felt and other materials, relative to protective headgear (Pp. 20. Droylsden, Manchester: British Hat and Allied Feltmakers Research Association, 1959). Other work, which has largely been in continuation of work already projected, has included further study of the carrotting of fur, an examination of the fibre properties of rabbit fur from different sources and attempts to assess the feltability of vials by simple tests that could be carried out in the factory. A theoretical study of the free oscillation of the beam system of the felt-hardening machine suggested that the pattern of behaviour when the weight is adjusted reflects the changes in the amplitude and natural frequency of vibration of the beam assembly. The experimental programme with selected polyethanoxy assistants in dyeing felt showed that the assistants were selective in action with acid-levelling, acid-milling and both 1 : 1 and 1 : 2 premetallized colours and even in a particular class. In studies of the relation between the size and shape of the hat body required to make hats of a given size, brim-width and crown-shape, wide differences were observed in the stretch pattern, and theoretical analysis indicated that the size and shape of hat bodies to give hats with a predetermined stretch pattern could be calculated if the geometry of the stretching could be stabilized. A review of the system of TDM indexes for measuring felt quality showed that the dependence of physical properties upon form weight changed with time and that periodic revision of the indexes was required to avoid obsolescence. A revised system has been proposed, while further work on frictional properties has provided an explanation of faults in felt which developed when bodies were pounced wet. Lists of publications, officers and staff are included.

"A Microsomal Malic Dehydrogenase"

Dr. Kenneth H. Shull writes: "It has come to my attention that three errors were made in my communication under this title in *Nature*, **183**, 259–260, January 24, 1959. In both Figs. 1 and 2 the sentence in the legends referring to the abscissæ should read 'The abscissa is the reciprocal of the substrate (oxalacetate) concentration in $\mu M \times 1{,}000/3$'. The value of the Michaelis constant, *Km*, line 24, column 2, p. 259, should read $4{\cdot}66 \times 10^{-5}$ *M*. The oxalacetate concentration, line 9, p. 260, should read 253 μM. These errors arose from the fact that I plotted units of mass, micromoles of oxalacetate per cuvette, rather than units of concentration. Since each cuvette contained a total volume of 3·0 ml., these reciprocal values for concentration are too large by a value of 1,000/3. The Michaelis constant which was determined graphically from Fig. 1 is thus too small by this same factor".

Announcements

Sir Gavin de Beer will retire from the directorship of the British Museum (Natural History) on April 30. He will be succeeded by Dr. T. C. S. Morrison-Scott, at present director of the Science Museum, and previously on the staff of the British Museum (Natural History) in charge of the Mammal Room.

No. 11, Vol. 5 (November 1959) of "The Bibliography of Scientific Publications of South and South East Asia", compiled jointly by Unesco Science Co-operation Offices for the area and published by Modec, National Physical Laboratory, New Delhi, contains a further 608 classified entries.

The second Asian/Pacific Congress of Cardiology will be held in Melbourne during the last week in May. Further information can be obtained from Dr. A. E. Doyle, Alfred Hospital, Melbourne, S.1, Victoria, Australia.

La Société de Chimie Physique is arranging a meeting on the Structure of Graphite and the Kinetics of its Reactions during May 31–June 3. Further information can be obtained from the Secrétaire Général de la Société de Chimie Physique, 10 Rue Vauquelin, Paris-V^e^.

The series of Summer Schools in Theoretical Chemistry which are held annually at Oxford is being continued this year during September 10–24, under the direction of Prof. C. A. Coulson. Further particulars can be obtained from the Assistant Secretary, Delegacy for Extra Mural Studies, Rewley House, Wellington Square, Oxford. Applications should be made before April 30.

A symposium on Molecular Structure and Spectroscopy will be held at the Department of Physics and Astronomy, Ohio State University, during June 13–17. There will be discussions of the interpretation of molecular spectroscopic data as well as methods for obtaining such data. In addition, there will be sessions devoted to those phases of spectroscopy of current interest. Further information can be obtained from Prof. R. A. Oetjen, Department of Physics and Astronomy, Ohio State University, Columbus 10, Ohio.

A two-day conference, to be held in Philadelphia during April 28–29, on "The Role of Nuclear Propulsion in our Future Merchant Marine", has been arranged by the Atomic Industrial Forum, an association of the atomic industry in the United States, in co-operation with the U.S. Atomic Energy Commission and the Maritime Administration. The provisional agenda includes: economics of nuclear ships, safety and liability problems, progress in foreign nations, and future prospects for the U.S. programme. Further information can be obtained from the Conference Manager, Atomic Industrial Forum, 3 East 54th Street, New York 22.

SCIENCE IN CIVIL LIFE IN BRITAIN

TWO recent debates in Parliament are of special interest for the further light thrown on the Government's intentions with regard to the Minister for Science. The first of these, in the House of Commons on December 7, was the outcome of a supplementary estimate not exceeding £4,080 for the Office of the Minister for Science for 1959–60, moved by Sir Edward Boyle, Financial Secretary to the Treasury. Sir Edward explained that this addition to the original Vote of £36,090 covered the remaining cost for the staff of the Atomic Energy Office and the Lord President's Office, and in particular the new provision for a chief information officer and supporting staff and provision of additional staff for the former Lord President's Office. He pointed out that Lord Hailsham's responsibility for the Atomic Energy Authority is in a sense a reversion to an earlier practice; but his responsibility for the four great executive research councils involves a considerable volume of Government expenditure; for the Department of Scientific and Industrial Research, the current expenditure, he said, is £13·25 million; for the Medical Research Council £3·5 million and for the Agricultural Research Council, just under £6 million. The Atomic Energy Authority accounts for £55 million current and £37 million of capital expenditure. The Minister for Science is also responsible for the Advisory Council on Scientific Policy and its Scientific Man-power Committee, the Overseas Research Council, and the Steering Group for Space Research; and Sir Edward Boyle emphasized the close relation of the Advisory Council for Scientific Policy both with the National Research Development Corporation and with defence science, and said that Lord Hailsham has already asked the Council to advise him on the balance of our national scientific effort. Within the four main research councils there are 97 research stations and establishments, and Lord Hailsham attaches great importance to links between these establishments and the universities and technical colleges, and will surely make these links and relations as fruitful as possible.

So far as defence research is concerned, the care of such activities, especially in the field of aircraft, guided weapons and electronics, are to be transferred from the former Minister of Supply to the new Minister of Aviation; but the responsibilities of the Minister for Science for space research will ensure very close contact with this work. Sir Edward also anticipated that the Minister would use the establishments of the research councils to reinforce the work of numerous Ministries and give them general guidance and advice in matters of scientific policy; but he suggested that the greatest challenge of all is to ensure that modern ideas and discoveries in science and technology are effectively and rapidly applied in British industry, and in this he thought development contracts may prove of service.

In the debate, some doubts were expressed as to the adequacy of the scientific staff in the Minister's office, and Mr. A. Greenwood, while welcoming the tribute paid to the Advisory Council on Scientific Policy, referred to the failure to implement the Council's recommendation regarding a national scientific reference library and suggested that the Council might need a stronger secretariat and an intelligence unit of its own. He and almost every speaker in the debate was critical of the absence of a spokesman for the Minister in the House of Commons. Sir Arthur V. Harvey referred to the need for greater co-ordination, mentioning especially the Faery rotodyne and Jodrell Bank Experimental Station. Mr. A. Albu stressed the need for much more money for basic research and for carefully selecting the lines of development on which our resources should be concentrated. Mr. Robert Carr suggested that the Minister might look into the possibility of stimulating research in industry through research contracts, and was concerned as to the possibility of too great a split between defence science and civil science under Government control. He also stressed the need for an adequate supply of technicians and skilled workers, and hoped that before long one Minister, instead of the present six, would answer in the House of Commons for the Minister for Science. Both Mr. Facey-Jones and Mr. Chuter Ede referred to the importance of full publication, Mr. Ede pointing out that secrecy is the great enemy to the progress of science, and Mr. D. Price stressed the value of an understanding of science in the Civil Service.

The Minister of Education, Sir David Eccles, replying on the debate, was able to show good reason why he should reply for the Minister for Science, particularly in view of his responsibilities for the schools and technical colleges. He believes there is a good prospect of reaching our target of 20,000 scientists and technologists. Although we are still short of science teachers, the numbers in grammar and technical schools are improving, and in 1959–60, 865 graduates in science entered university departments of education compared with 639 two years ago. He thinks that the Minister for Science will collect and co-ordinate relevant views on the controversial issues of scientific man-power, and place his conclusions before the education departments, universities, other scientific bodies and industry, and that he would be in a better position than any other Minister or agency to form estimates of the scientific resources and needs of Great Britain. The appointment of a Minister for Science has inevitably created some awkward administrative problems, but with good will there is no reason why they should not be settled.

The second debate, on science in civil life, opened by Lord Taylor in the House of Lords on December 9, is of greater interest because it provoked a further account from Lord Hailsham himself of his conception of his post as Minister for Science. Lord Taylor, after pointing out that it was no new thing for a senior Minister to be in charge of the main civil scientific Departments, referred more particularly to medical science and expressed the opinion that the Medical Research Council is a model of Government intervention in the sciences. Nevertheless, he thought that too much paper work comes to the Council for final decisions, and that the Council sometimes fails to try out new ideas outside the conventional run of thinking; he also suggested that besides, as a broad principle, backing good men, it might more often suggest the problems to be tackled. In this connexion,

Lord Taylor named three specific projects and then referred to a third difficulty arising in relation to the universities, through the shortage of endowed readerships and research professorships, and the consequent loss of good research workers in the medical field to clinical medicine. Universities, he said, are also unwilling to recognize Government research units and organizations as approved places for study for higher degrees, and he mentioned specifically research hospitals or hospitals with a specialized research unit. Like several subsequent speakers, he urged the need for a great effort in the social sciences, and suggested the establishment of a research council for the social sciences.

Lord Hailsham welcomed Lord Taylor's suggestions as illustrating the immense range of opportunity, and, replying to a specific question about scientific attachés, said that a fifth scientific attaché would be appointed, this time in Moscow. Dealing with the question in its broadest aspects, he said that the relation between Government and science and technology in all its aspects is one of the great challenges to the present Parliament. He himself is anxious to be as accessible as possible to members of both Houses, and insisted that the creation of his post was an evolutionary rather than a revolutionary step, and that no one should be dogmatic about the direction in which this kind of organization would lead us. Of his Ministry, he observed that there are only 39 people concerned with the expenditure of some £112 million of public money, and the executive work is carried out by scientists with a relative freedom, though subject to Government direction of one kind or another.

Looking further at the nature of the challenge to which he referred, Lord Hailsham said that science is not something which can be disentangled and treated separately from life. The approach of a scientific society and the need to learn how to operate this society and understand what it means involves talking in terms of generations rather than parliaments. What we do and say about a scientific society must be set against the present background: perhaps twenty or thirty years of intensive education, training and effort have been required to produce the men upon whom ultimately this kind of progress in human knowledge will depend. Lord Hailsham pointed out that this small group of pioneers needs the support of much more scientific literacy in the governing elements of the country and accordingly of our whole society, and he stressed the importance of the educational system developing such literacy. Science also has to be sustained by an immense army of skilled craftsmen and technicians, and while the Government must be responsible for the whole and for finding and strengthening the weak places, this must also be the joint responsibility of all concerned with the administration of any part of our society. Above all, scientific work must and can only be administered by scientists. Lord Hailsham also said that the distinction between the various defence and civil sciences is wholly artificial and arbitrary, and that scientists would see in a Minister for Science a real assurance that the civilian applications of science would not be overlooked because of the greater expenditure on defence projects. Science and scientists are not solely concerned with national things, and the values of the scientist are not purely material. Replying to Lord Morrison, Lord Hailsham firmly vindicated the creation of his office as Minister for Science; but he thought the proposal for a social science research council might be premature. He agreed with Lord Adrian as to the importance of an adequate supply of technicians in order to ensure efficient use of the services of scientists and technologists, though this presents some difficulty at the universities, and he also agreed as to the importance of sciences that do not fall into the normal classification. The Advisory Council on Scientific Policy has already been asked, in looking at the general balance of the scientific effort in Britain, to pay special attention to oceanography, seismology and astronomy and the relative stress to be placed on biology. He also firmly maintained the soundness of the decision to limit our effort in space research and emphasized the importance of international co-operation in this field. He agreed with Lord James of Rusholme as to the importance of science teaching, and that although accommodation is less important than the provision of teachers, it could become a limiting factor and therefore requires attention. Lord Hailsham hoped that during the coming session in Parliament there will be some debate on the size of universities and their contribution to our scientific effort, and that the present debate would be only the first of many on science in civil life.

SCIENCE AND FOREIGN POLICY IN THE UNITED STATES

In the years since the Second World War, non-military scientific developments have played important parts on the international stage. With technology accelerating at an amazing rate, what effects will it have on foreign relations problems in the future? Can we look ahead and try to ascertain what science will produce, and then take advantage of the product in foreign policy planning? These were questions posed by the Committee on Foreign Relations of the United States Senate (*Research for Industry*, 11, No. 6, Nov.–Dec., 1959). Stanford Research Institute scientists in all divisions provided assistance to Eugene Staley and Guy Benveniste in attempting to find some of the answers. The team indicated in its report that, while some future scientific developments may help solve foreign policy problems, the net effect of technological progress in the next decade is likely to be to create or intensify such problems. Thus, the security and well-being of the United States calls for a re-appraisal of present effort with the view of directing more energy toward non-military foreign policy challenges. Foreign policy planning should include continual review of scientific advances and their significance for international relations.

A specific suggestion was to establish a research and development office in the Federal Government oriented to identifying problems in newly developing countries and then stimulating research on these problems. In addition, an international development year might be organized along the lines of the International Geophysical Year with the aim of assisting

newly developing nations on a grand, concerted scale. In order to utilize science and scientists to facilitate understanding between nations, a United Nations weather and climate agency might be established to carry on research and ultimately to have authority over all weather and climate control undertakings. A United Nations university or system of universities could be dedicated to the advancement of science and the humanities. Other suggestions envisaged are the creation of an international translation and scientific information centre, and the establishment of adequate facilities to conduct research on technical problems of disarmament.

This study is the second of fifteen the Senate Relations Committee has authorized to examine United States foreign policy. It is designed to provide the Committee with background information, and the members are free to accept or reject the findings. The chairman, J. W. Fulbright, has announced that public hearings will be held later "to receive testimony from all interested parties in order to test the soundness of the findings and recommendations in all the studies undertaken".

NUTRITION IN EUROPE

A SYMPOSIUM on "Education and Training in Nutrition in Europe", arranged by the Food and Agriculture Organization of the United Nations and the World Health Organization through its European Regional Office, was held in Bad Homburg, West Germany, during December 2–11 1959. There were some sixty participants from twenty-two European countries, with Israel and Tunisia also represented. They belonged to a number of professional groups and included nutritionists, dietitians, physicians and public health officials, educationists, home economists and agronomists. The symposium was, in fact, designed to secure an inter-disciplinary approach.

The Food and Agriculture Organization and the World Health Organization are both concerned with nutrition; the former because its basic objective is to satisfy nutritional needs by making the necessary foods available, the latter because of the relation of nutrition to health. For many years they have collaborated in programmes and projects in this field, under the guidance of a joint expert committee. The meeting in Bad Homburg was one of a long series of joint undertakings.

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Lord Taylor named three specific projects and then referred to a third difficulty arising in relation to the universities, through the shortage of endowed readerships and research professorships, and the consequent loss of good research workers in the medical field to clinical medicine. Universities, he said, are also unwilling to recognize Government research units and organizations as approved places for study for higher degrees, and he mentioned specifically research hospitals or hospitals with a specialized research unit. Like several subsequent speakers, he urged the need for a great effort in the social sciences, and suggested the establishment of a research council for the social sciences.

Lord Hailsham welcomed Lord Taylor's suggestions as illustrating the immense range of opportunity, and, replying to a specific question about scientific attachés, said that a fifth scientific attaché would be appointed, this time in Moscow. Dealing with the question in its broadest aspects, he said that the relation between Government and science and technology in all its aspects is one of the great challenges to the present Parliament. He himself is anxious to be as accessible as possible to members of both Houses, and insisted that the creation of his post was an evolutionary rather than a revolutionary step, and that no one should be dogmatic about the direction in which this kind of organization would lead us. Of his Ministry, he observed that there are only 39 people concerned with the expenditure of some £112 million of public money, and the executive work is carried out by scientists with a relative freedom, though subject to Government direction of one kind or another.

Looking further at the nature of the challenge to which he referred, Lord Hailsham said that science is not something which can be disentangled and treated separately from life. The approach of a scientific society and the need to learn how to operate this society and understand what it means involves talking in terms of generations rather than parliaments. What we do and say about a scientific society must be set against the present background: perhaps twenty or thirty years of intensive education, training and effort have been required to produce the men upon whom ultimately this kind of progress in human knowledge will depend. Lord Hailsham pointed out that this small group of pioneers needs the support of much more scientific literacy in the governing elements of the country and accordingly of our whole society, and he stressed the importance of the educational system developing such literacy. Science also has to be sustained by an immense army of skilled craftsmen and technicians, and while the Government must be responsible for the whole and for finding and strengthening the weak places, this must also be the joint responsibility of all concerned with the administration of any part of our society. Above all, scientific work must and can only be administered by scientists. Lord Hailsham also said that the distinction between the various defence and civil sciences is wholly artificial and arbitrary, and that scientists would see in a Minister for Science a real assurance that the civilian applications of science would not be overlooked because of the greater expenditure on defence projects. Science and scientists are not solely concerned with national things, and the values of the scientist are not purely material. Replying to Lord Morrison, Lord Hailsham firmly vindicated the creation of his office as Minister for Science; but he thought the proposal for a social science research council might be premature. He agreed with Lord Adrian as to the importance of an adequate supply of technicians in order to ensure efficient use of the services of scientists and technologists, though this presents some difficulty at the universities, and he also agreed as to the importance of sciences that do not fall into the normal classification. The Advisory Council on Scientific Policy has already been asked, in looking at the general balance of the scientific effort in Britain, to pay special attention to oceanography, seismology and astronomy and the relative stress to be placed on biology. He also firmly maintained the soundness of the decision to limit our effort in space research and emphasized the importance of international co-operation in this field. He agreed with Lord James of Rusholme as to the importance of science teaching, and that although accommodation is less important than the provision of teachers, it could become a limiting factor and therefore requires attention. Lord Hailsham hoped that during the coming session in Parliament there will be some debate on the size of universities and their contribution to our scientific effort, and that the present debate would be only the first of many on science in civil life.

SCIENCE AND FOREIGN POLICY IN THE UNITED STATES

In the years since the Second World War, non-military scientific developments have played important parts on the international stage. With technology accelerating at an amazing rate, what effects will it have on foreign relations problems in the future? Can we look ahead and try to ascertain what science will produce, and then take advantage of the product in foreign policy planning? These were questions posed by the Committee on Foreign Relations of the United States Senate (*Research for Industry*, 11, No. 6, Nov.–Dec., 1959). Stanford Research Institute scientists in all divisions provided assistance to Eugene Staley and Guy Benveniste in attempting to find some of the answers. The team indicated in its report that, while some future scientific developments may help solve foreign policy problems, the net effect of technological progress in the next decade is likely to be to create or intensify such problems. Thus, the security and well-being of the United States calls for a re-appraisal of present effort with the view of directing more energy toward non-military foreign policy challenges. Foreign policy planning should include continual review of scientific advances and their significance for international relations.

A specific suggestion was to establish a research and development office in the Federal Government oriented to identifying problems in newly developing countries and then stimulating research on these problems. In addition, an international development year might be organized along the lines of the International Geophysical Year with the aim of assisting

newly developing nations on a grand, concerted scale. In order to utilize science and scientists to facilitate understanding between nations, a United Nations weather and climate agency might be established to carry on research and ultimately to have authority over all weather and climate control undertakings. A United Nations university or system of universities could be dedicated to the advancement of science and the humanities. Other suggestions envisaged are the creation of an international translation and scientific information centre, and the establishment of adequate facilities to conduct research on technical problems of disarmament.

This study is the second of fifteen the Senate Relations Committee has authorized to examine United States foreign policy. It is designed to provide the Committee with background information, and the members are free to accept or reject the findings. The chairman, J. W. Fulbright, has announced that public hearings will be held later "to receive testimony from all interested parties in order to test the soundness of the findings and recommendations in all the studies undertaken".

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knowledge so imparted is inter-linked and becomes an 'integrated' whole. On the training in nutrition now given to medical students, the views of those present at the symposium were unfavourable; it was noted that while students receive some instruction in the science of nutrition in its clinical aspects, this is not given in an 'integrated' way and is rarely related to the everyday problems of family life.

Emphasis was placed on the contribution to popular education which can be made by the public health nurse through her contacts with families in their homes. Home economists, a growing professional group in a number of European countries, can also influence families directly. As part of her work to improve family living conditions, the home economist is concerned with the planning of the family budget, the preparation of family meals, the domestic production, storage and preservation of food.

The training in nutrition of school teachers, so that they can teach its elements to their pupils, at an impressionable age, was discussed at some length. Ways of including nutrition in the teaching of subjects such as biology, health education and home economics were outlined, and it was agreed that it should not form a special and separate addition to school curricula. The need for simple and practical instruction was stressed, and attention was directed to the educational value of school meals.

Since good nutrition depends on the supply of enough of the right sort of food, it was appropriate for the symposium to consider the training in nutrition of agronomists and agricultural extension workers and their role in national nutrition programmes. Students in agricultural colleges learn much about the feeding of animals, but practically nothing about the feeding of human beings, which is after all the *raison d'être* of their profession.

Finally, the educational specialists present insisted that their colleagues should glance at modern educational techniques and modern ideas about the learning process, pointing out how these can be applied in the nutritional field. They were heard respectfully by a group in general more familiar with old-fashioned methods of instruction.

The symposium was aware that some of its conclusions cannot be exactly applied to the different countries represented, but require adaptation to the circumstances and needs of each. In the animated discussions, however, a large measure of agreement was reached on major points. Throughout, the friendly atmosphere characteristic of international technical meetings prevailed. W. R. Aykroyd

ELECTRON–PHONON INTERACTIONS

A CONFERENCE on Electron–Phonon Interactions in Solids was held at the Clarendon Laboratory, Oxford, during December 17–18. The Conference was held under auspices of the Physical Society and the delegates were welcomed by Dr. K. A. G. Mendelssohn (Oxford) on behalf of the President of the Society. The subject-matter of the Conference was of a very specialized nature and the organizers had further restricted the field of discussion by excluding topics directly related to superconductivity. It was therefore most encouraging that more than one hundred delegates attended the Conference. Among these were visitors from the United States, Belgium, Canada, Holland, South Africa and Switzerland. These delegates were not all specialists in the subject-matter of the conference, but nevertheless the discussions which followed the formal papers were often lively and to the point.

The Conference devoted its attention to those aspects of electron–phonon interactions which are most closely concerned with the complicated processes usually classified as 'transport phenomena' in metals and semiconductors. Examples of such phenomena are the electrical and thermal conductivities or the thermo-electric effects. The classical kinetic theory of the 'free electron gas' gives a very simple and elegant explanation of most of these effects in a first approximation. However, this theory makes the very fundamental assumption that the electron gas is in thermal equilibrium at some particular temperature, but does not clearly describe a mechanism by which this equilibrium can be achieved. The approach to equilibrium is discussed in terms of 'collisions' which do not involve interactions. The difficulties of a more rigorous theoretical treatment were emphasized by Dr. G. V. Chester (Birmingham) and Dr. J. M. Ziman (Cambridge). Dr. Chester, in attempting a more rigorous approach using the 'adiabatic' approximation, was rather surprised when experimentalists in his audience pressed him for some numerical orders of magnitude. Dr. Ziman reviewed the different methods at present used for estimating the electron–phonon interaction. He suggested that the strength of this interaction in metals was related to the Fermi energy; but the discussion which followed Dr. Ziman's paper showed that some delegates thought that he may have over-simplified the problem by laying such stress upon one parameter—the closeness of approach of the Fermi-surface to the Brillouin-zone boundary.

Prof. F. J. Blatt (Michigan State University), Dr. D. K. C. Macdonald (National Research Council, Ottawa), and Dr. J. R. Drabble (General Electric Co.) presented papers dealing with experimental investigations of thermo-electric effects in metals and semiconductors. Prof. Blatt described an interesting series of experiments which had been carried out using alloys of zinc, germanium, cadmium, indium, tin and antimony with copper. Of these alloys, 1 per cent zinc or germanium alloyed with copper gave a change in the thermo-electric power consistent with the expected phonon drag contribution estimated from pure copper. On the other hand, the addition of 1 per cent cadmium, indium, tin or antimony to copper reduced the phonon drag contribution almost to zero by virtue of phonon scattering arising from the solvent mass difference.

On the morning of the next day, Dr. A. B. Pippard (Cambridge) gave a simplified theoretical treatment of the anomalous absorption of ultrasonic waves by conduction electrons when the metal is situated in a magnetic field. Ultrasonic waves are essentially very long wave-length phonons, so that this technique provides in principle a direct approach to electron–phonon interaction processes. Unfortunately, this anomalous absorption is difficult to measure and is

often masked by other attenuating mechanisms such as may arise from the movement of dislocations. The effect sought for has apparently only been observed in copper and possibly in lead. Other papers during the morning were contributed by Dr. R. Furth (London) and Dr. L. Mackinnon (Leeds).

The session during the afternoon was opened by Dr. S. Raimes (London), who gave a careful account of the description of transport phenomena in metals using the techniques of plasma theory. This was followed by a paper in which Dr. R. J. Elliott (Oxford) directed attention to an alternative line of investigation which might provide useful information about electron–phonon interactions. He suggested that further electron-spin resonance experiments should be undertaken with metals in order to measure the electron spin-lattice relaxation time in more detail. The final paper was given by Dr. D. M. S. Bagguley (Oxford). He described some experiments using cyclotron resonance techniques to investigate the different collision processes for carriers in germanium.

All the delegates who attended the conference were grateful to the organizers for their efforts in providing an opportunity for listening to the formal papers and for informal discussions between colleagues. Such informal discussions are themselves a sufficient and complete justification for a conference of this nature. D. M. S. BAGGULEY

BRITISH GELATINE AND GLUE RESEARCH ASSOCIATION

THE eighteenth meeting of the Research Panel of the British Gelatine and Glue Research Association was held on November 12 with Mr. J. N. Blake (Richard Hodgson and Sons, Ltd.) in the chair. Mr. Blake introduced Dr. D. A. Sutton, who had recently succeeded Mr. A. G. Ward as director of research.

Dr. J. E. Eastoe (Department of Dental Science, Royal College of Surgeons of England) presented the first paper entitled "Bone—The Structure of a Biological Microcosm". After considering bone as one of the several mineralized biological tissues, note was taken of its occurrence in the vertebrate subphylum of the chordate phylum. Dr. Eastoe discussed bone at descending orders of size beginning with the skeleton, its function and the integration of its component parts, and continuing through the cellular level to electron microscope studies of bone mineral and collagen and thence on to the organization at the molecular level of these two main components. He concluded with a discussion of the hypotheses advanced to explain mineralization. Particular reference was made to the work of Glimcher, Hodge and Schmitt showing that mineralization is induced from metastable solutions containing calcium and phosphate only when the collagen fibrils present have the 640-Å. spacing, and that deposition can be prevented by traces of polysaccharide components. Chemical differences exist between bone and skin in that the former contains less polysaccharide and that its lysine and hydroxylysine have ε-amino groups more reactive towards fluorodinitrobenzene according to recent work by Solomons and Irving.

In the second paper, "Shrinkage of Cherries in Jelly", Miss M. J. Anthistle (Fruit and Vegetable Canning and Quick Freezing Research Association) demonstrated that the shrinkage which has been noted on storage can be virtually eliminated by adjustment of the surrounding gelatine gel (isoelectric *p*H, 4·7) to about *p*H 4·0; below this *p*H shrinkage occurred and above it a slight degree of swelling. The effect was not dependent on the sugar concentration. Miss Anthistle then considered the phenomenon in terms of the Donnan membrane equilibrium theory and deduced that shrinkage should be minimal at the isoelectric *p*H of the gelatine; in fact, it was minimal between *p*H 4·0 and 4·5. The *p*H of minimum shrinkage is thus somewhat lower than the isoelectric *p*H of the gel. In the discussion, it was suggested that the slight discrepancy might be due to an effect upon the equilibrium caused by the protein and pectin inside the fruit.

A short paper was then given by Mr. A. M. Kragh (British Gelatine and Glue Research Association) entitled "The Equilibrium Moisture Content of Plasticized Gelatine Gels". Glycerine and a sugar mixture (4 sucrose : 1 glucose) were used as plasticizers and relative humidities of between 35 and 93 per cent were studied. Temperature had a negligible effect upon the equilibrium moisture contents. Unless the relative humidity was very high, the equilibrium moisture content of the mixtures did not vary greatly over a wide range (0·5 : 1–4·0 : 1·0) of plasticizer : gelatine ratios. D. A. SUTTON

INTERLINGUA

THE free circulation of ideas and information is not less important for science than the circulation of the blood is for the body. This circulation is impeded by the publication of the results of scientific research in a multiplicity of languages. At least 50 per cent of the scientific literature of the world is published in languages that more than 50 per cent of the scientists of the world are unable to read. The number of published articles is growing rapidly; chemical literature, for example, has doubled itself in the past eight and a half years. There is also an increasing number of international meetings. There is thus not only the difficulty of reading published articles but also that of participating in discussions with research workers from other countries.

According to Forrest F. Cleveland, the scientist has two requirements. First, he has to scan the current literature to obtain ideas and information with respect to new developments in his field. Secondly, he must read in detail those articles that pertain to his own investigations. These requirements are largely frustrated by the language barrier (*American Scientist*, **47**, No. 3, 1959). Scientific work would be facilitated if the results of scientific research were published in a single language that every scientist would be able to read at sight. Such

a tool of intercommunication became available with the publication in 1951 of the "Interlingua–English Dictionary" and the "Interlingua Grammar" (Storm Publishers, 80 East Eleventh Street, New York 3). This was the culmination of twenty-seven years of research by the International Auxiliary Language Association in New York. Interlingua was developed by taking the words of vocabularies of the European languages (including English), standardizing or rationalizing them to remove regional irregularities and peculiarities, and constructing a simple grammar for use with the resultant vocabulary. An international language was obtained, which in a large measure is already in use and which can be read practically at sight by every educated person. The basic criterion for the acceptance of a word for the Interlingua vocabulary is that it must be present in corresponding forms and with corresponding meanings in at least three of the four language units: (1) Italian, (2) Spanish, and/or Portuguese, (3) French, and (4) English—with German and Russian as possible substitutes.

Impressed by the easy readability of Interlingua, Cleveland began, in May 1952, the publication in this language of a small periodical, *Spectroscopia Molecular*. It contains brief reports of new research results, summaries of important articles in the current literature, reports of spectroscopic meetings, reviews of new books, a calendar of future spectroscopic events, details about new instruments, and news about spectroscopists and recent developments. The experience of this small periodical provides a proof of the utility of Interlingua for intercommunication in the world of science.

Perhaps the greatest use of Interlingua to date has been in medicine. More than twenty medical journals publish extracts in Interlingua with all their original articles. In addition, Interlingua has been used for summaries in the programme of seven international medical congresses. *Science News Letter* publishes each month a summary in Interlingua of recent scientific developments.

To assist editors and authors who wish to study the possibility of increasing the extension of their work by the use of Interlingua, Science Service, Inc., has established an Interlingua Division. This is located at 80 East Eleventh Street, New York 3, and is under the direction of Dr. Alexander Gode.

RESEARCH AND DEVELOPMENT

CAN the effectiveness of research and development be measured? More precisely—given a certain amount of research effort, in a given field, can the rate at which useful results will emerge be predicted? These are some of the questions asked during a recent intensive study, "Basic Research in the Navy," carried out for the Naval Research Advisory Committee by Arthur D. Little, Inc. (Industrial Bulletin of Arthur D. Little, Inc., 369, Nov. 1959). In its report to the Secretary of the Navy, the Committee recommended further "research on research"; one approach is through a mathematical model describing the mechanisms of discovery and application.

The model describes a two-stage process; in the first stage, knowledge is discovered, and brought from the realm of the unknown into the known. In the second stage, combinations of the known facts are fitted together and applied. Formulation of the inventive process in this way emphasizes one important point: for every invention there is a key fact, or relation, or principle—the last to be discovered of all those necessary before the invention could be made. From this it follows that the date of discovery of this key fact is the earliest date upon which the invention could be made at all—although, of course, many inventions are not made until long after the discovery of the key fact.

There is a body of available knowledge, containing a certain number of key facts, corresponding to an equal number of possible inventions. If no new knowledge is added by research, these represent all the inventions which can be made. But the more research effort is applied, the more new facts come to light. It is also proportional to the size of the pool of (undiscovered) knowledge. The consequences of this ratio are interesting; the equation describing the rate of depletion of basic knowledge—the unknown subject—is an exponential decay curve like that used to describe the rate of decay of a radioactive substance. This is the model for the first stage of the research process.

The second stage concerns the application of discovered facts through invention. Here again the rate of progress is proportional to the amount of effort expended and to the size of the pool of knowledge—in this case, the number of discovered, but unapplied, facts. Yet a fact may be applied many times, in different combinations with other facts. It is not the unit of knowledge that is important—rather, it is the conclusions drawn from a number of units. To determine a rate for the second stage properly, one must invoke the techniques of modern algebra.

There is, also, the question of the time-lag between discovery and application; for the second stage, as well as the first, one can draw an analogy with the process of radioactive decay. The body of known but unapplied facts is considered, on this model, to have a well-defined half-life, but the expected time for any one fact to be applied may range from very short to extremely long. The expected half-life itself is a variable quantity which depends on the amount of effort expended on development work.

By putting these various factors together, for the second stage an S-shaped curve is obtained indicating first a slow rate of application, then a more rapid increase, and finally a plateau; curves of this type are familiar to economists for describing the development of a market or a new product. This is the model for the inventive process, and it is confirmed by observation.

Perhaps the most interesting feature of the model is that an optimum ratio for the effort to be applied to the two stages of discovery and application of knowledge can be derived. That is, one can in theory answer the question: For maximum productivity of a research programme, what percentage of the budget should be devoted to basic research, and what part to applied research? The model suggests that to develop one large and complex field, basic research should not fall below about 20 per cent of the total research budget.

UNITED KINGDOM HOSPITAL LIBRARY SERVICES

A PILOT survey of hospital library services has been made by an independent committee, of which Mr. J. A. M. Ellison-Macartney was chairman, sponsored by the King Edward's Hospital Fund for London (Hospital Library Services: a Pilot Survey. Report of an Independent Committee sponsored by King Edward's Hospital Fund for London. Pp. 56. London: King Edward's Hospital Fund for London, 1959. 2*s*. 6*d*.). Its report, now published, directs attention to the apathy of some hospital authorities and officials and to the inadequacy of much accommodation, but the greatest weakness uncovered by the survey was the quality of the books provided by the smaller voluntary organizations. The Committee believes that ideally the public libraries should be the major source of supply of books and that this should become a recognized function and duty of all such libraries. Nevertheless, the survey also revealed the great strength which lies in the supply of voluntary librarians, and the Committee also believes that ideally the staffing of hospital libraries could be undertaken by voluntary organizations in conjunction with the local public libraries supplying the majority of the books.

In general, hospital library services require a new look, and the Committee recommends that hospital authorities at the highest level should regard it as an essential duty to see that an efficient service is provided in all hospitals (except where special circumstances render it undesirable) rather than leave the decision to be taken at a lower administrative level. Far greater positive interest in the library service should be taken at all levels of hospital authorities and staffs; it should no longer be left in the main to voluntary helpers with the minimum of support in interest, funds and equipment. All architects' plans for new hospitals or extensions to existing hospitals should in future include library accommodation conveniently sited, and certain standards for accommodation and equipment are recommended for consideration. In particular, it is emphasized that because most library services are likely to continue to be run by volunteers, particularly women of middle age, the siting of library accommodation, height of shelves, weight of trolleys, heating, lighting and ventilation are of paramount importance. The standard of books provided should be that of books provided to the general public by the best public libraries, and the Committee recommends that for a hospital of average size, annual expenditure on new books should be not less than 6*s*. per bed. All hospital library services should include the provision of books to hospital staffs, and the Committee suggests that valuable training courses run by St. John–Red Cross should be open to all hospital librarians. The question whether books are capable of carrying tuberculosis infection requires scientific investigation and an authoritative pronouncement. The Committee believes that with the existing variety of library services, full efficiency cannot be attained on a basis of less than £1 per bed per annum at present prices, or £3 per bed per annum if salaries, but not overheads, are included.

THE ATLANTIC EEL PROBLEM

RECENTLY Tucker[1] published his view on the origin of the European eels. He advocates the revolutionary theory that all the European eels are the offspring of American parent stock. His argument is presented under three headings, of which the first, dealing with the return of the silver eels towards their breeding places, is in my opinion the most important one. Therefore, special attention will be paid to this section of Tucker's article.

Tucker begins by laying stress on the fact that the European silver eel is already well advanced towards being a reproductive oceanic fish despite the long journey which supposedly lies before it, this in marked contrast with the American silver eel, which is relatively retarded. The conclusion is drawn that this is just the reverse of what one would anticipate, taking into consideration the distance it has to go.

The impossibility of providing exact information on the time required to become a reproductive fish renders this subject elusive of criticism and debate. Comparison with other species of fish is moreover of little value; one should in my opinion concentrate on the features and habits of the European silver eel itself.

For the same reason the next paragraph dealing with the comparison of external features of both species under consideration cannot lead to an irrefutable conclusion. The only reasonable conclusion one could draw from the differences mentioned is, in my opinion, that there is every reason for believing in the existence of two really distinct species, which is just the opposite of what Tucker tries to demonstrate.

According to Tucker, the longevity of silver eels in captivity is irrelevant. We know, however, that the silver eels, kept in the tanks of the eel merchants, are always on the move; when the water in the tanks is in motion, the silver eels are swimming in the upstream direction. Despite the rather unfavourable conditions in the tanks, the silver eels go on swimming for months and months in succession. It is certainly a remarkable fact that such eels are, even after a period of prolonged storage, fat enough to be attractive for the consumer, for they can easily be sold at a fair price. This demonstrates that silver eels are able to move over huge distances without degeneration of their tissues. It seems therefore that this matter cannot be considered as irrelevant to the subject under discussion.

Two other items in Tucker's article are open to doubt:

(1) If one assumes with Tucker that the migrating eels must use a very simple orientation mechanism

based on currents, temperatures, and/or salinity conditions, and next, considering the complexity of the actual situation, concludes that such a system would fail to guide the eels to their supposed spawning grounds, this reasoning cannot be used as evidence to demonstrate that the eels will not reach such spawning grounds at all. Such a reasoning would indeed be comparable to the following: We assume that migrating birds orientate themselves on wind-direction and wind-strength. Since such a system cannot possibly guide the birds towards their destination, we find ourselves forced to conclude that birds do not reach their destination at all. Since we all know that the birds do reach their destination the only reasonable conclusion is that our assumption was not sound. Unfortunately we do not yet know how eels do manage to orientate themselves; but this also applies to birds: we do know for sure that they are capable of a perfect orientation but fail to understand just how.

(2) Tucker supposes that all European silver eels use the same pattern of behaviour and concludes that they therefore cannot all of them reach their destination. This conclusion is used to support his theory that European eels do not reach the Atlantic spawning grounds at all. Tucker, however, designs a migration system for the American silver eels; he finds himself forced to conclude that the Mississippi eels do not fit in this system. Tucker states then: "the fate of these need not concern us". If so, why does the fate of the Black Sea eels or the Baltic eels need to concern the migration system for the European eels? I fail to find any logic in such reasoning.

Tucker then proceeds by putting the following question: "The eels if they survived would be abundant. Why have they never been taken by research vessels in the open Atlantic or by the intensive fisheries along the Continental Slope? Are agility and this or that depth of swimming adequate explanations?" I can adduce the following evidence in reply to this question.

Despite the alleged rapid degeneration the silver eel is an agile and 'clever' fish, which is extremely difficult to catch. In the IJsselmeer, on which I have worked as fisheries biologist for fourteen years, focusing mainly on eel problems, the only practical way to catch silver eels is with stationary gear, that is, fyke nets. With eel trawls, silver eels cannot be caught, though such nets are very suited to the capture of younger stages. Using the newly improved IJsselmeer eel trawl—especially designed and suited for catching eels in huge quantities—in the area along the Afsluitdijk we did not catch one single silver eel, notwithstanding the fact that the area must have teemed at that time with silver eels according to the catches made with fyke nets in the immediate vicinity.

Now the IJsselmeer is a shallow body of water, where silver eels abound, and use was made of a small meshed net equipped with two non-returning funnels. These conditions contrast sharply with those in the open and much deeper seas and oceans where silver eels do not concentrate but are sparse and gradually disperse. Fishing is carried out here with dragged gear, which we already know is not capable of catching silver eels even if the eels do not swim at "this or that depth" but would move along the bottom, as Tucker obviously supposes, but of which we are not at all sure. Further, the sea trawls are not equipped with non-returning funnels and have a mesh size in the cod-end of about 7 cm., big enough to offer even the biggest eel the best chance for escape. No fisheries expert acquainted with these details could expect the catch of a single silver eel in open sea.

If on the contrary the European silver eels die on the Continental Shelf, as Tucker presumes, millions and millions of dying and dead silver eels would occur locally on the sea bottom year after year. Undoubtedly such eels incapable of escape would regularly be scooped up by the numerous trawls scraping the sea bottom. As this does not happen we are forced to conclude that silver eels do survive their trek over the Continental Shelf. It cannot even be supposed that they die in deeper waters in the vicinity of the Continental Shelf, for such deaths will not occur at a given spot or depth but will be scattered over quite a vast area, considering the distances to be covered and the range in the maturating process.

A further argument of Tucker is that there are several deeps in the Mediterranean and the Atlantic Ocean, which offer conditions apparently identical to those of the Sargasso Sea; yet eels do not spawn there. I would point out that we do not know anything of the conditions for reproductive activities required by the eels; moreover, Tucker's argument is of the same type as the following: Scandinavian chaffinches in reality observed to hibernate in Ireland will have to migrate over England (which indeed is what happens); but since these birds do not hibernate in England, which offers conditions apparently identical to those in Ireland, it is highly improbable that they will hibernate in Ireland.

Tucker's discussion of the conditions which the American silver eels meet has—as I have already stated—no relation to the achievements of the European silver eels.

Later in Tucker's article are some statements which are not backed up by any substantial data. This also applies to the 'evidence' which is supposed to show the 'debility' of the European silver eel which is 'obliged' to drift passively down stream with the currents. However inactive they are according to Tucker, they are without any doubt very capable of escaping a highly specialized eel-fishing gear dragged through the water with a speed of several miles per hour. Apart from this we must reckon with the possibility that silver eels will be dragged along by the current in the direction of the Sargasso Sea, for a fair current is running in the opposite direction under the Gulf Stream at a depth of some 2,800 m., showing velocities up to 17 cm./sec. (that is, about 15 km./day)[2–4]. I wonder whether Tucker has been aware of this fact.

Tucker discusses some consequences—with rather far-fetched explanations—of the supposed non-return of the silver eels to their spawning places. In this respect I might direct attention to the necessity of constant hydrographical features, especially water temperatures, in the Sargasso Sea from year to year and that during scores of centuries (cf. also ref. 5). It is difficult to believe in such a feature, for the rather short period for which records are available allows us already to conclude that hydrographical conditions are not constant at all but fluctuate quite considerably in the oceans. Therefore one cannot assume with Tucker that a constancy of water temperature has been the guiding factor in the eel's reproduction.

Finally I would direct attention to Tucker's statement that: "The proposition of Schmidt[4]

(p. 204, lines 20–40: How do masses of larvæ in the Western Atlantic sort themselves out . . . . ?) has led to misunderstanding especially among lay authors".

It is quite incomprehensible why such a simple question should lead to misunderstanding, but anyhow it would have been fairer also to quote Schmidt's own answer: "In the main, the question is no longer difficult to answer. In the case of the American eel, the pelagic larval stage is terminated in about one year; . . . . It is otherwise with the European eel, which takes nearly three times as long over its larval development, as a result of which practically all of them are far away from the Western (American) portion of the Atlantic when the time comes for them, as elvers, to seek the coasts".

Surely, there can be no difficulty in accepting the fact that only fully grown leptocephali after having arrived on the slope of a Continental Shelf will stay there. After having completed metamorphosis they will continue their migration as elvers. The sorting out of larvæ off America is in my opinion quite plausible: the fully grown larvæ, that is, those of the American eel, respond to continental conditions and stay; all the others, that is, those of the European eel, with still two years growth ahead, do not respond, and hence are carried on by the Gulf Stream.

I believe that the meaning of all this is quite evident: the edges of the Continental Shelf constitute the area where tidal streams begin. Simultaneous with metamorphosis into the elver stage, the animals change their behaviour in such a way that it enables them to respond to, and take advantage of, the possibilities which the tidal currents offer them, as Creutzberg[7] has recently discovered.

For the sake of completeness I wish to remark that this is not the only known case of eels staying for some time in a transition area, next changing their behaviour pattern in such a way that they will respond to the newly encountered conditions and then continuing their migration. I discovered myself[8] that this is what happens when elvers migrate from sea into fresh water. The well-known metamorphosis from eel into silver eel is also a clear indication that the eel is a real master in the opportunistic art of changing habits and taking advantage of new conditions.

It will be clear from the foregoing discussion that Tucker's claim that his hypothesis is at parity with Schmidt's cannot possibly be supported by me. I still feel that Schmidt is right in his opinion. Concerning the still rather mysterious orientation of silver eels towards the Sargasso Sea, I am inclined to assume that silver eels, having a tendency to develop into a deep sea fish[9–10], are provided with an orientation mechanism directed westward. After leaving the European Continental waters in a westerly direction, many of the silver eels will inevitably meet the deep Atlantic current under the Gulf Stream but in opposite direction. When this happens I do not see any reason why the silver eels should not make use of this current, which will guide them afterwards towards the Sargasso Sea.

Such a journey might be of some 7,500 km. length. Supposing that silver eels will swim at a low speed, for example, some 50 km./day, of which they undoubtedly are capable[11], it will take them only about 150 days to reach their destination. We may be sure that such an effort exerted during that rather short period will be far from demanding the utmost of the animals and will undoubtedly leave enough reserve material to allow an ample development of the gonads.

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DR. DEELDER is incorrect in referring to the American silver eel. This phase has not yet been observed, and the migratory stage is known as the bronze or black eel[1,2]. I understand from Dr. W. E. Frost that Dr. V. D. Vladykov recently identified the bronze phase as an intermediate stage between the yellow and silver in British eels.

The apparent maintenance of condition in 'stored' silver eels has already been discussed[3], together with the check on maturation imposed by artificially enforced life in fresh water[1]. 'Putte', the eighty-eight year-old Swedish eel, was in only partial nuptial dress when it died[4]. But under these conditions reserve fat, normally used for gonad maturation, locomotion and physiological (osmoregulatory) work[3], is available for swimming only and restricted swimming at that. It is not sufficient to observe vaguely that stored eels remain active and healthy and then claim that this "demonstrates irrefutably that silver eels are able to move over huge distances". We need concrete data on distances swum, speeds, weight-losses and analyses, preferably in salt not fresh water, and in the meantime it is more material that eels make the Baltic run at average speeds of between 5 and 10 miles per day and lose up to 20 per cent of their weight on the way[3,5].

The migrating bird argument is logical in itself but fallaciously applied. It is possible *a priori* to postulate and experimentally to demonstrate alternative methods of navigation in birds, and birds are known to arrive. It is possible *a priori* to reject all visual navigational aids in eels and, from our present knowledge of physics, oceanography and physiology, it is not possible to postulate any system other than one involving passive transport and inherent reactions to temperature and salinity gradients. Such a system could easily direct a majority of the American eels[1], but not the European: and European eels are not known to arrive.

"The fate of the Mississippi eels need not concern us"[1]. I was not forced to any conclusion whatsoever. Having shown a simple return route for the bulk of the American population I judged it immaterial and prodigal of space to deal withthe complicated Gulf of Mexico current system. Those who wish may study Dietrich[6] and evacuate their Mississippi eels through the Florida Current or through the more circuitous bottom currents of the Gulf and Caribbean. It is sufficient that we have put the major part of the American eels on to the spawning ground; we cannot devise any system that will put any section of the European population on to theirs.

Dr. Deelder's point about the IJsselmeer silver eel fisheries is well taken.

There is no real difficulty about the concealed mortality of silver eels in the sea, any more than there is with the normal mortality of herring, mackerel and all the other marine fishes. The sea has her predators to remove her sick, and her scavengers to keep her clean.

Since my comments on the fitness of the silver eel for migration have caused so much misunderstanding, I will now restate them.

The word 'debility' has been objected to by many other critics[3] besides Dr. Deelder, always through misinterpretation of its single appearance. The original text[1] reads: ". . . the debility of the (European) eel which is obliged to drift passively downstream in the current is due to demineralization . . . remineralization and resumed liveliness occur when the eel reaches the sea". Dr. Deelder chides me for lack of supporting data; I cited Bertin[7] (intending him to be read), who in turn gives a summary and bibliography of a dozen relevant papers by Fontaine and his school; both these authors also employ the word 'débilité' in the same context as I do, in relation to the late freshwater condition. There is no need for Dr. Deelder to attack with his IJsselmeer story; and is not the IJsselmeer still highly brackish?

The adequacy of the stored food-reserves to provide for the journey is open to speculation[1,3,8]. The vitality of silver eels in inshore waters, re-affirmed by D'Ancona[8], Jones[3] and now Dr. Deelder, is immaterial to the problem of the ocean crossing. We are not interested in the condition of local populations inshore. We want to know the state of the residual European population by the time it crosses the Continental Shelf and is well on its journey, and we have no direct evidence as to that. But I maintain that the cases already cited[1,3,8], of eels losing weight on the Baltic run; of near-ripe eels, eels with degenerating guts, an eel with a blocked vent, provide material evidence that Baltic eels are too far advanced when only partly on their way. The same argument applies to precocious individuals taken from the Mediterranean. I argue that the condition of these silver eels, at most a few hundred miles from their home streams, is a significant indication of the probable state of the survivors of the whole continental European population when an equivalent distance out to sea.

I have already discussed *Conger conger* as a biological indicator of identical spawning conditions in various deeps in the western and eastern Atlantic and Mediterranean[3]. Dr. Deelder's chaffinch argument is logically and biologically unsound, as well as inapplicable to the present situation, but it is nevertheless worth analysing. The British Isles have only the native *Fringilla coelebs gengleri*, but are invaded each autumn by the related Continental *F.c.coelebs* as a winter migrant; the reverse migration of *F.c.gengleri* does not occur. Competing for the identical ecological niche each sub-species must clearly have some advantage over the other in its normal range. Such competition with members of both sub-species compels *F.c.coelebs* flocks to move on across Britain and into Ireland, where a seasonal increase is noted[3]. Now, there can be no competition for food or territory among spawning eels; there are no breeding populations of *Anguilla* in the eastern deeps; why, therefore should *A. anguilla* make a plainly hazardous migration to an area in which its larvæ must enter into competition with those of at least seven other Apodal fishes[7,9,10]. I think it is destroyed by its own metabolic failure before it reaches any of the likely spawning deeps, near or far.

I am mystified by Dr. Deelder's expressed doubt regarding my knowledge of the counter-current beneath the Gulf Stream; I did, in fact, specify this very current as the likely vehicle for the returning American eels[1]. The said current, running as it does near the foot of the American Continental Shelf, is irrelevant to the European eel problem unless Dr. Deelder postulates a return route via the Norwegian Coastal Current, Jan Mayen, and the Greenland Current, and so along the American eel route, with a greatly increased distance/time factor and a northward movement rather than a westerly one as he now specifically suggests. It is interesting to note here that tagged eels released in the Elbe have recently been recovered off Denmark, indicating a northerly rather than a westerly migration[11]. Dr. Deelder's estimate of likely 'low' migration speeds is, like Jones's[3], much too high in relation to those observed[3,5].

I am aware of the annual fluctuations in hydrographical conditions, but do not think that the broad Atlantic picture has altered sufficiently in (geologically) recent times to affect the validity of the new eel hypothesis. As regards earlier epochs there are further intriguing problems in the origin of the Japanese *A. japonica* population (which is closely related to[12] and may have been derived from the Atlantic *Anguilla* during the last Central American subsidence, or during an opening of the North-West Passage), and in the relation between climate and vertebral numbers of the European fossil *Anguilla*.

There is no need to labour my comment on Schmidt's account of the 'sorting' of the two types of leptocephali. In my general preparatory reading I found that it had been misunderstood and given rise to erroneous reasoning, and attempted a re-statement for that reason. There was no intentional unfairness in not quoting the passage in full to save space; again, the reference was intended to be consulted. Here I would like to correct an impression in certain quarters that my new interpretation of Schmidt's work is in some way derogatory to his memory. Dr. Anton Fr. Bruun, *in litt.*, has generously exonerated me of any such charge. If it were not for the oceanic researches of Dr. Johannes Schmidt and the experimental researches of the late Dr. A. Vedel Täning, together with their other Danish colleagues, I would not have been able to write a word on this subject. Furthermore, most of the work which has been used in this re-assessment of the Atlantic eel problem was not published during Schmidt's lifetime.

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PROTECTION AGAINST ACUTE EFFECTS OF RADIATION BY HYPOXIA

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IT is well known[1] that the sensitivity of biological systems to radiation is increased in the presence of oxygen and decreased in its absence. In the case of whole-body irradiation of mammals, Dowdy *et al.*[2] have shown that exposure under reduced oxygen pressure results in a considerable increase of the *LD*50. In the course of a systematic study on the age factor in short-term and long-term effects of radiation[3], it occurred to us that the variation of radiation sensitivity with age, recently reported by us[4], may be associated with an oxygen effect. To test this hypothesis we investigated the survival of mice exposed to acute whole-body doses of radiation under hypoxic conditions. These measurements were carried out during April and May 1959, as a pilot experiment for a more detailed study of this effect in animals of various ages. Since, however, the completion of this investigation will take some time, it may be of interest to report our interim findings.

The mice used were of the same strain (albino *SAS*/4) as in the main experiment[3]. They were exposed in 'Perspex' containers consisting of twin cylinders, each of which could accommodate two mice. By means of tubes leading to a manifold, it was possible, by remote control, to substitute nitrogen for air in one of the cylinders. In this way four mice could be exposed simultaneously, two breathing air or oxygen and the other two nitrogen. To prevent convulsion of the mice while removing the oxygen, the mice were anæsthetized prior to irradiation. The anæsthetic used was pentobarbitone sodium ('Nembutal', Abbott Laboratories, Ltd.), at a dosage of 40 mgm. per kgm., administered intraperitoneally. No anæsthetic was used in the case of mice 1–3 days old, since they were not subject to convulsions under nitrogen. With this procedure we observed no ill effects of either the anæsthetic or the temporary hypoxia. Out of a total of 150 control mice which passed through the procedure of being anæsthetized and/or hypoxia, but without being given a dose of radiation, only two died in the course of thirty days.

The radiation used was the beam of 14-MeV. electrons from our linear accelerator. Electrons rather than X-rays were used to make it possible to deliver the required dose of radiation in a very short time. The mean dose-rate was about 2,500 rads per sec., so that even the highest dose employed could be delivered in less than a second. A broad electron beam was obtained by using an aluminium scatterer near the exit window of the accelerator. At a distance of 1 m., where the mice were placed, the beam was found to be uniform over the whole irradiated area.

For measurement of dose we used a small ionization chamber placed near the mice container. The dose absorbed was determined in two ways : (*a*) by a comparison of the readings of the ionization chamber with a 'Perspex' strip dosemeter which had been calibrated absolutely by a calorimetric technique[5], and (*b*) by calculating the collection efficiency of the ionization chamber and then making a correction for the conversion of e.s.u./c.c. into rads. These methods gave results in very good agreement with each other.

The experimental procedure, as determined by preliminary trials on the reaction of the mice to hypoxia, was as follows. After the container with the mice was placed into position for irradiation, the oxygen content was gradually reduced by admixture with nitrogen. This proceeded for 25 sec., by which time the gas was 100 per cent nitrogen flowing at a rate of 6 l. per min. The mice were kept in this atmosphere for 12 sec. ; at the end of this time the exposure was made and the nitrogen immediately replaced by oxygen or air.

Figs. 1 and 2 show the results obtained with mice aged 1–3 days and 4 weeks, respectively. The percentage of the animals dying within 30 days is plotted on probability paper against the dose to which they were exposed. These graphs illustrate the striking protective effect of temporary removal of oxygen. From these and other graphs, the *LD*50 values for the different experiments were determined and are given in Table 1. For the tests with older animals

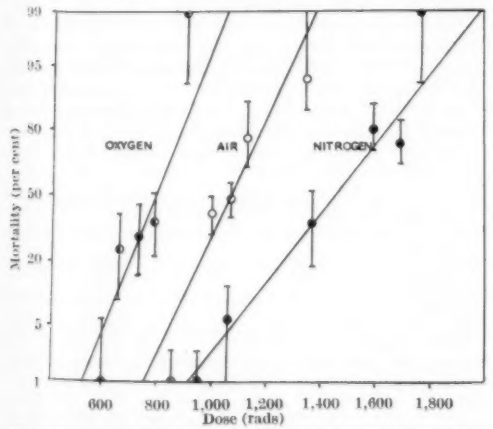

Fig. 1. Percentage 30-day mortality of mice 1–3 days old, breathing different gases, as a function of dose

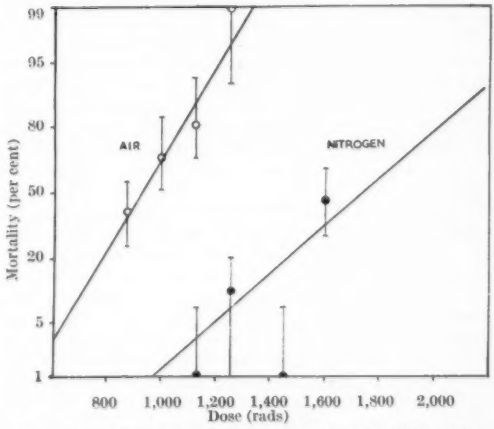

Fig. 2. Percentage 30-day mortality of mice 4 weeks old, breathing different gases, as a function of dose

Table 1. *LD*50 Values for Mice exposed under Different Conditions

Age	X-ray exposure in air (rads)	Electron exposure in: Oxygen (rads)	Air (rads)	Nitrogen (rads)	Nitrogen protection factor
1–3 days	833 ± 24	788 ± 18	1,068 ± 20	1,450 ± 40	1·74 ± 0·07
4 weeks	684 ± 16	—	930 ± 45	1,760 ± 90	2·58 ± 0·15
19 weeks	880 ± 25	—	1,005 ± 65	1,750 ± 150	1·99 ± 0·18
82 weeks	764 ± 20	—	950 ± 100	1,320 ± 120	1·73 ± 0·16

very few mice were available; hence the large experimental errors for these groups.

Table 1 also contains the *LD*50 values obtained previously[4] for mice exposed under the standard conditions of our investigation, namely, using 15-MeV. X-rays at a rate of 7 rads per sec. (The conversion factor used (1 r. = 0·98 rad) was obtained in a direct measurement under the conditions of the experiment.) The last column of Table 1 contains the nitrogen protection factor, that is, the ratio of the *LD*50 at exposure in nitrogen to that under standard conditions.

These results show that exposure of mice under hypoxic conditions produces an entirely different age variation from exposure in air. For example, at 4 weeks of age the *LD*50 reaches a minimum when the mice are exposed in air, but it appears to have its highest value at the nitrogen exposure.

It is not yet clear how the oxygen effect operates in this case, but it may arise from differences in oxygen tension in tissues of animals of different ages. The relatively high *LD*50 value during the first week of life may be the result of a reduced oxygen tension in the neonatal stage, due to incomplete pulmonary ventilation and to circulatory readjustments of early extra-uterine life[6]. Indirect evidence of a lower oxygen tension is provided in our experiment in which the neonatal mice were exposed in an oxygen atmosphere; this gave a considerable decrease of the *LD*50. At normal oxygen tension the change should have been very small.

The increase of the *LD*50 for mice older than 4 weeks could also be due to a gradual decrease with age of the oxygen tension in tissues, starting from about 4 weeks. Such a decrease might result from changes with age in vascularity, diffusion coefficients and pulmonary ventilation. It is known that large gradients of oxygen tension exist in tissues, but there is little evidence that they change with age; there is also no evidence to the contrary. Another possible explanation of the results obtained with the hypoxic mice is that the time required to reduce to a given level the oxygen tension in the vital tissues, such as bone marrow, may vary with age, becoming longer the older the animal. This would mean that in our experiments the older mice were exposed under less hypoxic conditions than the younger ones. Experiments are now in progress to measure directly the oxygen tension in various tissues in mice of different ages.

Referring to Table 1, it will be noticed that the *LD*50 values obtained in air in the present experiment are, in all cases, higher than those obtained previously. The main differences between this and the previous experiment are: (*a*) electrons were used instead of X-rays; (*b*) the dose-rate was much higher; (*c*) the animals were, in some cases, anæsthetized. It is difficult to see how the change from X-rays to electrons could make a significant difference, particularly since the dose absorbed within the body of the animal was uniform within a few per cent. In other experiments, too, we have found no difference in the effects produced by X-rays or electrons at comparable dose-rates.

There remain the two other factors. We have evidence that anæsthesia does reduce sensitivity to radiation, probably because of a lowering of the oxygen tension in tissues[7]. This may account for some of the increase in the *LD*50 in animals exposed in air.

With regard to dose-rate it is known that over a large range of dose-rates the sensitivity to radiation increases with increasing dose-rate[8,9]. Our own preliminary investigations at high dose-rates do not show an increase of sensitivity; there are, in fact, indications of a decreasing sensitivity with dose-rate. Such a decrease, if confirmed, might occur for the following reason. Oxygen in the tissues is consumed during irradiation, but is normally replenished from the oxygen in the blood. If, however, the dose is delivered at a very high rate, the loss due to the first fraction of the dose may not be made up quickly enough and the remaining dose is given to the animal while some sensitive parts of it are under hypoxic conditions. Dewey and Boag[10] have reported such an effect in bacteria; the results of Kirby-Smith and Dolphin[11], who studied the chromosome breakage of *Tradescantia*, may also be due to a similar effect. If the same applied to mammals, then both factors, the anæsthetic and the high dose-rate, would really be oxygen effects. It is quite likely that the dose-rate effect would become manifest only in combination with an anæsthetic or a naturally low oxygen tension in tissues.

Further experiments, particularly using animals of more age-groups, are needed to elucidate these problems. Even from these preliminary results, however, it is obvious that age is an important factor in the protective action of hypoxia as well as in the acute effects of radiation. The same may apply to long-term effects. We have indeed evidence (to be published shortly) that long-term effects of radiation, such as shortening of life, show a similar variation with age at irradiation.

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INTERPRETATION OF POTENTIOMETRIC TITRATION OF H-MONTMORILLONITE

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IT has been observed[1] that the *p*H titration curves of hydrogen clays with strong monovalent bases have various characteristics, such as variation in steepness of slope in different parts of the curve. Variations have also been noticed for the kind of clay mineral, the amount of mineral in suspension, and the cations used to produce neutralization. Garrels and Christ[2], using original data of Marshall and Bergman[3] for the titration of the clay mineral (beidellite) in the Putnam silt loam soil, have shown that the neutralization curve of *p*H plotted against concentration of potassium hydroxide appears similar to that of two independent clay acids. They termed the two substrates the C^- (centre or interlayer site) and E^- (edge site). Blackmon[4] calculated exchange constants for the C^- and E^- sites of beidellite and 'illite' for K^+, NH_4^+ and Na^+. Cations are more strongly held by the E^- than by the C^- sites.

Neutralization curves obtained with different clay minerals show variations that can, in part, be attributed to the ratio of C^- to E^- sites. Differences in the bonding energy of monovalent and divalent cations introduce another variable that is expressed by the shapes of the titration curves. The resemblance between neutralization curves of some clay minerals and of humic acid suggested that a similar explanation would apply to these two kinds of substances, that is, the neutralization of a polymeric electrolyte.

Katchalsky and Spitnik[5] showed that the neutralization of a polymeric electrolyte could not be described by the Henderson–Hasselbalch equation:

$$pH = pK_a + \log \frac{\alpha}{1 - \alpha}$$

where pK_a is the negative logarithm of the ionization constant of a weak acid, and α is the degree of neutralization. Katchalsky and Spitnik ascribe this deviation to the uncoiling of the polymer chains during titration because weak hydrogen bonds are replaced by strong cationic bonds as ionization proceeds. These authors have further shown that a generalized Henderson–Hasselbalch equation of the form:

$$pH = pK_a + n \log \frac{\alpha}{1 - \alpha}$$

where n is a constant, will describe the titration of a polymeric electrolyte. It was therefore of interest to determine whether the titration of H-montmorillonite with sodium hydroxide, which also involves a change of dimension of the substrate due to swelling, was similar to that of humic acid.

A sample of montmorillonite from Chambers, Arizona (A.P.I. Standard No. 23, ref. 6), was converted to the H-form by treatment in 1 *N* hydrochloric acid by the method of Aldrich and Buchanan[7], with the omission of the final treatment with an ion-exchange resin. Care was taken to remove all traces of chloride by repeated washing and centrifugation. No aluminium was found in the supernatant water in contact with the H-montmorillonite, although this water had a *p*H value sufficiently low for aluminium to be in solution. This suggests that no aluminium was in the exchange positions. Titrations were made by a discontinuous method in which 65-mgm. samples of montmorillonite were suspended in 5 ml. water and increasing multiples of a 0·02-ml. increment of 0·1 *N* sodium hydroxide were added. The maximum volume of sodium hydroxide used was 1·2 ml. Additional water was added, when required, to make a constant volume of 6·20 ml. for each sample. The *p*H value was measured repeatedly until it remained constant for about six weeks. Titration curves were plotted semi-logarithmically. The volume of titrant added was entered on the logarithmic ordinate, and the *p*H on the linear abscissa. The result is shown in Fig. 1.

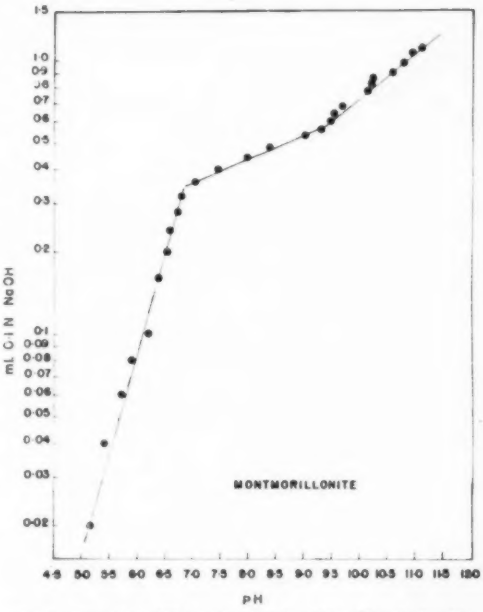

Fig. 1. Titration of H-montmorillonite with sodium hydroxide

The plot was made in this way for the reasons set out below. Gran[8] has shown that if a dibasic weak acid is titrated with a strong base the following relation holds before the first equivalence point is reached:

$$10^{-pH} = \frac{K_a}{V}(V_1 - V)$$

Here K_a is the first ionization constant of the acid, V is the volume of base added, and V_1 is the volume necessary to reach equivalence. Upon logarithmic transformation this relation yields:

$$pH = \log V - \log K_a - \log (V_1 - V)$$

This equation can be rearranged to:

$$pH = \log V - \log K_a - \log V_1 + \log (1 + \frac{V}{V_1})$$

a relation which shows that a plot of pH against log V will yield a straight line except for a deviation contributed by the last term in this equation. Evaluating log $(1 + V/V_1)$ we find that, at the start of the titration, $V = 0$ and log $(1 + V/V_1) = 0$, whereas at the point at which equivalence is reached, $V = V_1$ and log $(1 + V/V_1) = \log 2 = 0{\cdot}30$. Hence, a plot of log V against pH over this region will deviate from linearity by 0·30 pH units. This small deviation may be neglected.

In the region between the first and second equivalence points, Gran[8] showed that:

$$10^{-pH} = K'_a \frac{V_2 - V}{V - V_1}$$

where K'_a is the second ionization constant of the acid and V_2 is the volume of base necessary to reach the second equivalence point. By using the same approach as before, this equation can be rewritten as:

$$pH = \log (V - V_1) - \log K'_a - \log V_2 - \log (1 + \frac{V}{V_2})$$

and it is possible to plot pH against log $(V - V_1)$ as essentially a straight line.

A plot of log V against pH will also yield a straight line. Gran[8] has shown that, after the second equivalence point has been passed:

$$10^{pH} = \frac{C_B}{f_H K_w (V_0 + V)} (V - V_1)$$

where C_B is the concentration of base, f_H is the activity coefficient of the hydrogen ions, K_w is the ionization constant of water, and V_0 is the volume at the start of the titration. Again, it can be expected from this relation that also in this region a plot of log V against pH will yield a straight line.

If, then, log V is plotted against pH when a dibasic weak acid is titrated with a strong base, three approximately straight lines should appear. These lines should intersect at the equivalence points. A plot of V against pH, based on the discontinuous titration of H-montmorillonite showed that this is so for this clay mineral (Fig. 1). It is possible to estimate from the equivalence points in Fig. 1 that the cation exchange capacity of the first clay acid, presumably representing the interlayer (C^-) sites, is about 50 m.equiv./100 gm., and that the cation exchange capacity of the second acid, presumably representing the edge sites (E^-), is about 40 m. equiv./100 gm. The total exchange capacity of this H-montmorillonite as determined by this method is about 90 m. equiv./100 gm. The exchangeable cations remaining on this H-clay, as determined by the Association of Official Agricultural Chemists method[9], were 34 m. equiv./100 gm., and the total exchange capacity of the original montmorillonite was, therefore (90 + 34 m. equiv.)/100 gm. or 124 m. equiv./100 gm., a value comparing closely with that of ~ 120 m. equiv./100 gm. reported for this mineral[10].

A plot of log $\alpha/(1 - \alpha)$, values for which were easily obtained after the exchange capacity was determined, against pH over the region of the neutralization of the first acid gave a straight line with a slope of 1 and an intercept of 6·4 (Fig. 2*a*). A few points in the region where $1 - \alpha$ approached zero could not be used in the construction of this line. It appears from

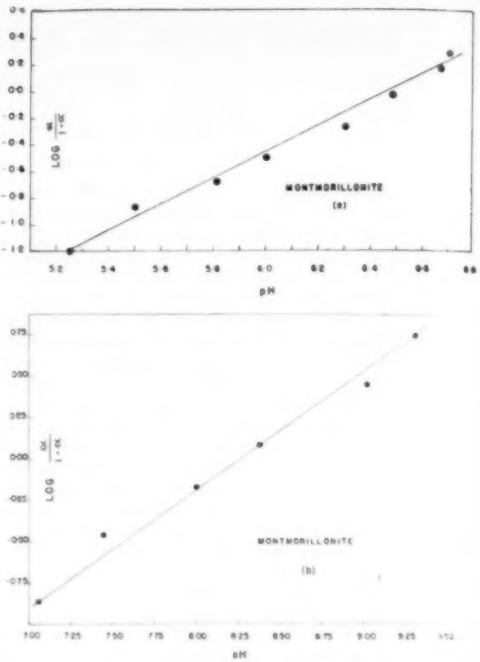

Fig. 2. (*a*) Plot of log $\alpha/(1-\alpha)$ against pH for first clay acid; (*b*) plot of log $\alpha/(1-\alpha)$ against pH for second clay acid

the value of the intercept that the ionization constant of the first acid is $10^{-6{\cdot}4}$ and from the slope that the acid behaves as a pure weak acid upon neutralization. A similar plot over the region of the neutralization of the second acid (Fig. 2*b*) gave a straight line with an intercept of 8·3, indicating an ionization constant of the second clay acid of $10^{-8{\cdot}3}$ and a slope of 0·7. This shows that the clay acid deviates in its behaviour from that of pure weak acid, and that it can be described by the type of generalized Henderson-Hasselbalch equation used in the titration of polyelectrolytes. The value of n in this case, however, is smaller than 1. The reason for this deviation has not yet been explored.

We think that plotting the results of discontinuous titrations of H-clays as described is a useful way to characterize their exchange relations. We have made similar titrations for vermiculite and 'illite'. These results, together with that for montmorillonite, will be described in a more comprehensive paper now being prepared for publication.

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CHEMICAL AND SEROLOGICAL RELATIONSHIPS OF CERTAIN BACTERIAL POLYSACCHARIDES CONTAINING SIALIC ACID

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SINCE the composition of the polysaccharide, colominic acid, obtained from an *E. coli* organism, was established[1] as poly N-acetylneuraminic acid (ovine sialic acid), reports have appeared describing other bacterial polysaccharides that contain a sialic acid[2,3]. One of these substances, the specific hapten of group *C N. meningitidis*[3], is also largely constituted of units of O-sialic acid. Thus, it appeared that colominic acid may be produced by species of bacteria other than *E. coli*. It was of interest to ascertain by agglutination tests whether the various species of bacteria known to produce polysaccharides rich in sialic acid showed any relationship to each other. In addition, a study was made of the chemical and serological properties of four polysaccharides containing sialic acid obtained from different bacteria.

All enteric bacteria were grown in sterile culture. The bottles containing 15 l. of suitable medium were incubated (with aeration) at 37° C. for 18 hr. The bacteria were killed by the addition of 100 ml. of chloroform and harvested by centrifugation. The cells were suspended in 100 ml. of water and collected as before. The washed bacteria were suspended in 100 ml. of water and lyophilized.

N. meningitidis bacteria were cultivated at 37° C. for 18 hr. on 10 sterile blood agar plates. The cells were carefully removed by flushing each plate with 5 ml. of distilled water. The cells were collected by centrifugation, washed, and lyophilized.

Sialic acid analyses were performed on the dried bacteria, employing a modification of Werner and Odin's method[4]. N-acetylneuraminic acid served as the standard and the figures recorded represent typical values, expressed as a percentage of dry weight: *Escherichia coli* 01 : *K*1 : *HNM* (0·27); *E. coli* 02 : *K*1 : *HNM* (0·46); *Neisseria meningitidis* group *C* 1908 (0·64); *N. meningitidis* group *C* 1935 (0·26); *Citrobacter freundii* (1·92); *Salmonella dahlem* (1·19); and *S. djkarta* (0·51).

Antibacterial antisera prepared against the *K* antigen of the *E. coli* strains were obtained by Edwards's procedure[5]. *N. meningitidis* antibacterial antisera were prepared by Rake's method[6]. Edwards and Ewing's method[7] was used for production of *H* antigen antibacterial antisera prepared against the *C. freundii*, *S. djkarta* and *S. dahlem* strains.

The results of the agglutination tests are given in Table 1. It is to be noted that all the bacteria show agglutination in homologous antisera. The *E. coli* 01 : *K*1 : *HNM* and the group *C N. meningitidis* 1908 strains are unrelated by cross agglutination tests to each other or to any of the other strains examined. The cross agglutination tests reveal a relationship between the two *Salmonella* strains and

Table 1. Agglutination of Bacteria containing Sialic Acid in Homologous and Heterologous Antisera

Organism tested	Antibacterial antiserum	Dilution of antiserum										
		1/5	1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1,280	1/2,560	1/5,120
S. djkarta	*S. djkarta*	4+	4+	4+	4+	4+	4+	4+	4+	4+	1+	±
S. dahlem		4+	4+	4+	4+	4+	4+	2+	1+	±		
C. freundii		4+	4+	4+	4+	3+	2+	0	0	0	0	0
E. coli 01 : *K*1 : *HNM*		0	0	0	0	0	0	0	0	0	0	0
N. meningitidis group *C* 1908		0	0	0	0	0	0	0	0	0	0	0
S. djkarta	*S. dahlem*	4+	4+	4+	4+	4+	4+	4+	3+	2+	0	0
S. dahlem		4+	4+	4+	4+	4+	4+	4+	4+	4+	3+	2+
C. freundii		4+	4+	4+	4+	4+	2+	0	0	0	0	0
E. coli 01 : *K*1 : *HNM*		0	0	0	0	0	0	0	0	0	0	0
N. meningitidis group *C* 1908		0	0	0	0	0	0	0	0	0	0	0
S. djkarta	*C. freundii*	4+	4+	4+	4+	4+	4+	4+	4+	4+	1+	0
S. dahlem		4+	4+	4+	4+	4+	4+	4+	4+	4+	1+	0
C. freundii		4+	4+	4+	4+	4+	4+	4+	4+	4+	4+	4+
E. coli 01 : *K*1 : *HNM*		0	0	0	0	0	0	0	0	0	0	0
N. meningitidis group *C* 1908		0	0	0	0	0	0	0	0	0	0	0
S. djkarta	*E. coli* 01 : *K*1 : *HNM*	0	0	0	0	0	0	0	0	0	0	0
S. dahlem		0	0	0	0	0	0	0	0	0	0	0
C. freundii		0	0	0	0	0	0	0	0	0	0	0
E. coli 01 : *K*1 : *HNM*		4+	4+	4+	4+	3+	2+	+	0	0	0	0
N. meningitidis group *C* 1908		0	0	0	0	0	0	0	0	0	0	0
S. djkarta	*N. meningitidis* group *C* 1908	0	0	0	0	0	0	0	0	0	0	0
S. dahlem		0	0	0	0	0	0	0	0	0	0	0
C. freundii		0	0	0	0	0	0	0	0	0	0	0
E. coli 01 : *K*1 : *HNM*		0	0	0	0	0	0	0	0	0	0	0
N. meningitidis group *C* 1908		4+	4+	4+	4+	4+	4+	2+	2+	1+	0	0

Table 2. Composition of Polysaccharides containing Sialic Acid obtained from Various Bacteria

Source organism	Substance isolated	Empirical formula	Elemental analysis					Per cent sialic acid
			C	H	N	O	CH_3CO	
E. coli 01 : *K*1 : *HNM*	Colominic acid	$(C_{11}H_{19}NO_9)_n$	42·83	6·46	4·79	45·97	14·45	99·0
E. coli 02 : *K*1 : *HNM*	Colominic acid	$(C_{11}H_{19}NO_9)_n$	43·75	6·36	4·71	45·18	13·88	98·5
N. meningitidis group *C* 1935	Group *C* hapten	$(C_9H_{15}NO_8)_n$	41·80	6·66	5·32	46·24	11·62	85·0
C. freundii	Polysaccharide	$(C_{16}H_{29}N_3O_{11})_n$	44·19	7·16	6·86	41·79	10·57	36·2

between each of these with the *C. freundii* organism. Cross agglutination tests, not recorded here, show that *E. coli* 02 : *K*1 : *HNM* is related to *E. coli* 01 : *K*1 : *HNM* and to no other strain listed in Table 1. Furthermore, a group *C N. meningitidis* strain known as 1935 is related only to the group *C N. meningitidis* 1908 strain and to none other listed here. Therefore, on the basis of these tests the above bacteria which produce polysaccharides that contain sialic acid can be divided into three groups.

Polysaccharides containing sialic acid were isolated from members of each group. Colominic acid was isolated from the culture media of *E. coli* 01 : *K*1 : *HNM* and 02 : *K*1 : *HNM* bacteria by a previously reported procedure[8]. This procedure, with a few modifications, was employed for the preparation of a new polysaccharide that contains sialic acid isolated from the culture medium of the *C. freundii* organism.

The results of the chemical analyses are recorded in Table 2. It is to be noted that colominic acid isolated from either *E. coli* 02 : *K*1 : *HNM* or 01 : *K*1 : *HNM* bacteria has similar elemental compositions and sialic acid content with one acetyl group for each nitrogen atom. Furthermore, identical infra-red absorption spectra and optical rotation values are obtained. N-acetylneuraminic acid is the only substance found in hydrolysates of either polymer. The calculated empirical formulæ support the belief that O-sialic acid ($C_{11}H_{19}NO_9$) is the sole chemical constituent present in these polysaccharides.

Group *C* hapten isolated from group *C N. meningitidis* 1935 strain contains about 85 per cent sialic acid. An empirical formula $(C_9H_{15}NO_8)_n$ also fits the elemental analytical data reported[2].

The group *C* hapten 1908 used in the present study contains 70·4 per cent sialic acid and a small amount of protein[9]. Hexosamines[10] are absent. The results of these tests indicate that a portion of the group *C* hapten is undetermined.

The *C. freundii* polysaccharide contains 36 per cent sialic acid and one of the nitrogen atoms is believed to be acetylated. Hexuronic acids are absent and only trace amounts of protein can be detected. About 21 per cent of hexosamine is present. Phosphorus is absent. Thus, half this polysaccharide, rich in nitrogen, remains to be characterized.

All four polysaccharides readily decompose upon heating in dilute mineral acid to form humin. Colominic acid does not form precipitins with antibacterial antisera prepared against *E. coli* 01 : *K*1 : *HNM*, 02 : *K*1 : *HNM* or group *C N. meningitidis* 1908 and 1935 bacteria. The group *C* hapten yields a precipitin with the group *C N. meningitidis* antibacterial antisera in a dilution of 1 part in 10^6 but not with the *E. coli* 01 : *K*1 : *HNM* or 02 : *K*1 : *HNM* antisera. Incubation of colominic acid with *N. meningitidis* 1908 or 1935 antisera fails to block precipitin formation by the group *C* hapten. Incubation of group *C* hapten with *E. coli* 01 : *K*1 : *HNM* or 02 : *K*1 : *HNM* antibacterial antiserum followed by the addition of *E. coli* 01 : *K*1 : *HNM* or 02 : *K*1 : *HNM* bacteria does not inhibit agglutination of the cells.

Hæmagglutination tests employing group *C* hapten adsorbed to human O erythrocytes in group *C N. meningitidis* 1908 or 1935 antisera show strong hæmagglutination of the cells. However, no hæmagglutination occurs with *E. coli* 01 : *K*1 : *HNM* or 02 : *K*1 : *HNM* antibacterial antisera. Incubation of colominic acid with either *N. meningitidis* antiserum prior to the addition of the coated erythrocytes fails to block hæmagglutination of the cells. Therefore, it must be concluded that on the basis of the serological tests the group *C* hapten obtained from group *C N. meningitidis* organisms is unrelated to colominic acid obtained from *E. coli* bacteria despite the chemical similarity of the two materials. The absence of a serological relationship suggests differences in chemical linkage between the constituent units.

The *C. freundii* polysaccharide gives a precipitin with antibacterial antisera prepared against *C. freundii*, *S. djkarta* and *S. dahlem* bacteria.

Up to the present time the sialic acids have been found only in Gram-negative organisms. Three polysaccharides containing sialic acid obtained from such organisms—colominic acid from *E. coli*, group *C* hapten from *N. meningitidis* and a previously undescribed material from a *C. freundii* organism—were found to contain different amounts of sialic acid and to be unrelated on the basis of serological tests. Colominic acid remains as a unique material produced only by *E. coli* organisms which possess a *K*1 antigenic serotype[11]. Precipitin tests indicate that a polysaccharide rich in sialic acid obtained from a *C. freundii* organism is related to a similar material produced by *S. dahlem* and *S. djkarta* bacteria. Thus, the occurrence of the sialic acids in various bacterial polysaccharides in different chemical combinations indicates that these monosaccharides are common structural constituents of cells.

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We are indebted to Dr. H. Scherp, National Institutes of Health, Bethesda, Maryland, and to Dr. G. Watson, Bowman Gray Medical School, North Carolina, for the sample of group *C* hapten 1908 and for the group *C N. meningitidis* 1908 and 1935 strains.

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LETTERS TO THE EDITORS

RADIOPHYSICS

Constant Ionosphere Height for Audio-frequency Propagation

THE wave-form of an atmospheric, resulting from a distant lightning flash to Earth, has variously been interpreted in terms of pulse reflexion between parallel or concentric conducting Earth and ionospheric layers[1,2] or as pulse dispersion during propagation in the region between these same layers[3]. Recent papers[4,5] have discussed the equivalence of these approaches. In each case the Earth–ionosphere separation and the storm distance are the principal determinants of the positions of the peaks of the trace. Within certain limits these propagation parameters may be estimated from the observed wave-forms.

Smooth type wave-forms[5] of distant Atlantic origin, received both by day and night, have recently been studied extensively at Nottingham. Wave-form analyses of 70 traces, using wave-guide concepts, together with distance estimates in the range 1,750–5,000 km., kindly provided by the Meteorological Office Sferics network, have permitted estimation of the effective ionosphere height both by day and for several hours after sunset in the case of winter-time storms. A constant ionosphere height of 83 ± 2 km. irrespective of the time of day was the most reasonable conclusion from the results available, with no significant variations from this mean value for individual recording periods and no suggestion of a systematic variation with the onset of night-time conditions even up to 4 hr. after local sunset. This suggests a fundamental difference between smooth and reflexion type wave-forms, for the latter of which various workers[1,2] have reported an increase in effective height at night.

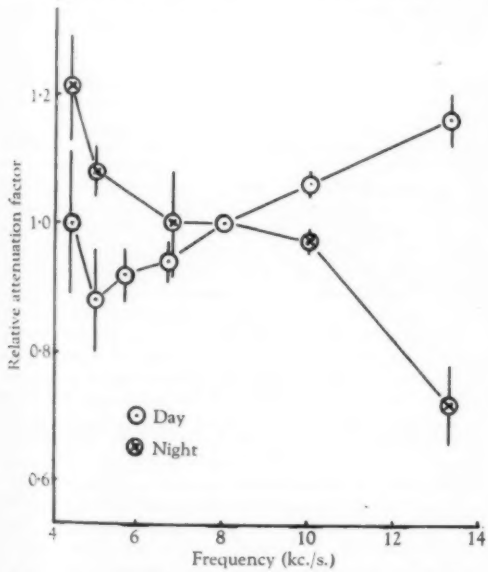

Fig. 1. Attenuation factors. (Fractional changes per 1,000 km. relative to 8 kc./s.)

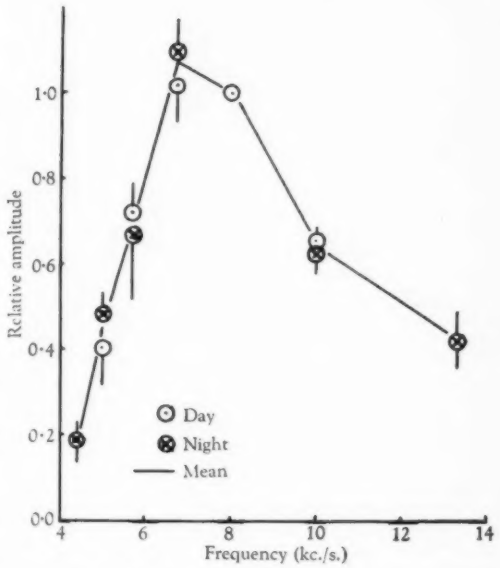

Fig. 2. Average source spectra

An earlier paper[5] has discussed the derivation of relative attenuation coefficients for propagation and the mean amplitude-spectrum at the source from statistical analysis of the oscillation amplitudes throughout the observed wave-forms. For a group of 150 apparently regular smooth type wave-forms, it was found that attenuation factor per 1,000 km. relative to that at 8 kc./s. varied little throughout the frequency-range 4–14 kc./s. A slight systematic increase with frequency was noted by day and a less precise and regular decrease at night (Fig. 1). The corresponding source spectra were indistinguishable (Fig. 2).

The very slight diurnal variation of attenuation in the appropriate frequency band, while unexpected when comparison is made with previous atmospherics measurements[6], might have been predicted from the very close similarity of day- and night-time forms of this restricted group of smooth type wave-forms. The identity of the day and night source spectra provides gratifying confirmation of the analysis and the significance of its conclusions.

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Jan. 20.

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Measurement of Solar and Diurnal Effects in the High Atmosphere by Artificial Satellites

In a previous investigation[1] atmospheric densities had been derived from the orbital elements[2] of the satellites 1958 β 2, 1958 α, 1958 δ and others, and reduced to the mean altitude of the perigee by means of the Kallmann–Juncosa[3] model. A good correlation exists between atmospheric fluctuations and the 20-cm. solar flux curve[4]. This is apparent not only from the 'monthly' fluctuations[5] but also from long-period variations extending over several months. For altitudes of 660, 350 and 210 km. the relation between density and solar flux is approximately linear for values of solar flux S between 100 and 240×10^{-22} W./m.^{2} c./s. To demonstrate the effect it was necessary to separate quantitatively the suspected diurnal fluctuations and the fluctuations caused by variable solar radiation. A preliminary investigation was carried out using the geocentric angular distance perigee–Sun which had already been employed by Jacchia (see ref. 2) for comparison with the satellite data. The angular distance proved very useful so long as no separation of the diurnal and terrestrial effects was possible. One expected, however, the atmospheric density to be dependent on $\Delta\alpha = \alpha_\pi - \alpha_\odot$, $\Delta\delta = \delta_\pi - \delta_\odot$ and the geocentric latitude ψ of the perigee (where α is right ascension, δ is declination, π is perigee, $\odot$ is Sun).

A separation of the diurnal effect (dependence on $\Delta\alpha$) is now possible for the satellite 1958 β 2, for which the best observational data are available. The result is presented in Figs. 1 and 2. For this purpose the atmospheric density data were first reduced to a standard value of the solar 20-cm. radiation ($S = 190 \times 10^{-22}$ W./m.^{2} c./s.). This was possible because of the linear relation between atmospheric density and 20-cm. radiation which had already been found[1]. The resulting values were drawn in a $\Delta\alpha$, $\Delta\delta$ co-ordinate system and the lines of constant density determined. They are shown in Fig. 1 for values of 2, 4, 6, 8 and 10×10^{-16} gm. cm.$^{-3}$. For simplification in the diagram, the individual values are represented in groups (see right-hand corner of diagram). The dotted line represents $\delta_\pi = 0$ ('perigee above the equator'). The lines of constant density are strongly influenced by the scattering of the individual values. For this reason only the general appearance of the curves can be considered reliable. From this appearance one can deduce two effects: (1) a seasonal effect (dependent on the declination of the Sun) with a maximum value of atmospheric density at $\Delta\delta = 0$; and (2) a terrestrial effect with a maximum value of the density above the equator. The two effects are superposed.

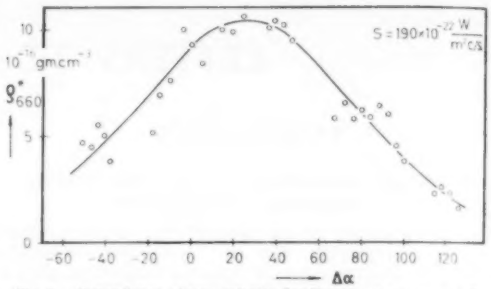

Fig. 2. Dependence of atmospheric density on $\Delta\alpha = \alpha_\pi - \alpha\odot$ in the equatorial zone (diurnal effect)

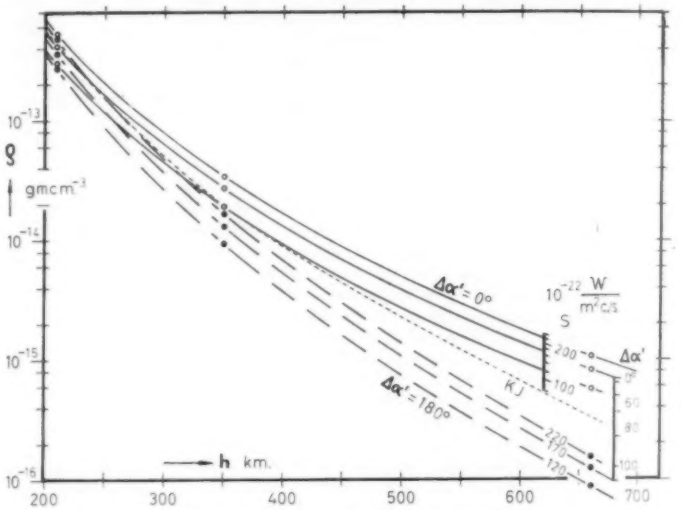

Fig. 3. Model of air density derived from the orbital elements of the satellites 1958 β 2, α and δ 2 with solar and diurnal effects ($\Delta\alpha' = \Delta\alpha - 25° = 0°$ and 180° corresponding to 13h. 40m. and 1h. 40m. local time). The short dotted line (*KJ*) represents the model by Kallmann and Juncosa (ref. 3)

Most conspicuous is the strong diurnal variation of $\Delta\alpha$ (Fig. 2) and the phase shift of about 25° corresponding to a maximum value of atmospheric density around 13h. 40m. true local time. The value of the delay is somewhat uncertain[1]. Using a simplified method for analysing the results, we found[1] a shift of 16°. Wyatt[6] found 23° (1h. 30m.) and an asymmetric diurnal variation. The asymmetry may result from the fact that in his derivation all values were included independent of variations in $\Delta\delta$ and ψ. If only values of the density from a narrow zone around the equator are used with both

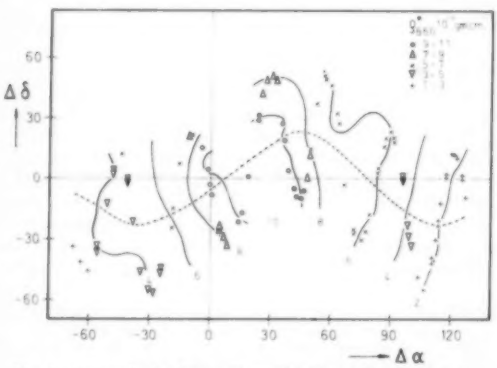

Fig. 1. Atmospheric density at an altitude of 660 km. in a co-ordinate system centred at the subsolar point. $\Delta\alpha = \alpha_\pi - \alpha\odot$, $\Delta\delta = \delta\pi - \delta\odot$ (α, right ascension; δ, declination; π, perigee; $\odot$, Sun). The values of atmospheric density are reduced to a flux of solar 20-cm. radiation of $S = 190 \times 10^{-22}$ W./m.^{2} c./s.

$|\psi| < 30°$ and $|\Delta\delta| < 30°$, a much smaller scattering of the results is found. In our earlier paper (ref. 1, Fig. 3), some points did not fit the general curve. It was found that all of them represent density values for which $|\Delta\delta| > 30°$.

Using atmospheric densities as derived in our earlier communication[1] for altitudes of 210, 350 and 660 km. we obtain a density model with solar and diurnal fluctuations as shown in Fig. 3. The scale-heights of the atmosphere according to Kallmann and Juncosa[2] on which the computations were originally based are eliminated from the final result by means of an iteration process (see ref. 1).

In Fig. 3 the three upper curves (solid lines) are valid for $\Delta\alpha' = \Delta\alpha - 25° = 0°$ (13h. 40m. local time); the three lower (dotted) curves are valid for $\Delta\alpha' = 180°$ (extrapolated values). In each group the lowest of the three curves corresponds to a value of $S = 120$, the middle curve to $S = 170$ and the upper curve to $S = 220 \times 10^{-22}$ W./m.^{2} c./s. of the solar 20-cm. radiation. The large density fluctuation between day and night suggests a daily up and down movement of the atmosphere[6].

A layer of constant atmospheric density, for example, would rise from 520 to 660 km. within 6h. according to Fig. 2. The resulting velocities in the vertical direction are about 25 km./hr. The air movements decrease with decreasing altitude and at 200 km. become insignificant compared with the fluctuation caused by solar radiation. The latter must originate in a layer below 200 km. This suggests that the absorption of solar X-ray radiation in the E-layer of the ionosphere is responsible for them. The scale height $H = \frac{RT}{gM}$ (where R is the gas constant, T is temperature, g is acceleration of gravity, M is mean molecular weight) of the atmosphere and thus the ratio T/M changes strongly with the time of the day but very little with the flux of 20-cm. radiation.

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PHYSICS

Natural Radioactivity of Samarium and Neodymium

There seems to exist a discrepancy between the measured value of the alpha-decay half-life of natural samarium (samarium-147) and the theoretical half-life calculated from its measured alpha energy[1]. This may be due to the fact that in most ion-chamber measurements of samarium-147, heavy natural alpha-emitters with much higher energies have been used as standards, which leads to great difficulties because of the non-linearity of the ionization process.

In this investigation thin samples containing about 50 μgm./cm.^{2} of natural samarium, 0·3 μgm./cm.^{2} of natural uranium and 0·5 μgm./cm.^{2} of elemental boron were analysed in a grid-type ionization chamber in the presence of a thermal neutron flux of $1·5 \times 10^3$ n/cm.^{2} obtained from a polonium–beryllium source.

The neutrons absorbed by boron gave rise to alpha-particles with energies of 1·797 and 1·474 MeV.[2], respectively, which were recorded photographically together with the samarium and uranium alpha-particles for the purposes of calibration[3].

By the use of exposures several days long, spectra containing 10^4–10^5 pulses were obtained and analysed with a spectrophotometer. The result for the alpha energy of samarium-147 is:

$$E = 2·20 \pm 0·03 \text{ MeV.}$$

which is somewhat higher than the value quoted by W. Jesse and J. Sadauskis[4].

The specific activity of samarium-147 was measured by counting the alpha-particles from 28·9 mgm. of samarium which were vacuum-evaporated on a source plate of diameter 200 mm. Taking into account self-absorption and back-scattering, a value of $7·00 \pm 0·3$ counts/min./mgm. of natural samarium is obtained, which corresponds to a half-life of $(1·14 \pm 0·05) \times 10^{11}$ yr. for the isotope 147.

An attempt to detect the natural alpha activity of neodymium was made using a 200-mm. source-plate on which 36 mgm. of neodymium were evaporated. In spite of appreciable thorium contamination a weak line was observed at $(2·0 \pm 0·1)$ MeV., in agreement with investigations made by the emulsion method[5].

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Evaporation Figures on the Surface of Sodium Chloride Crystals

Figures which appear during evaporation on the surface of sodium chloride have already been reported by E. Kern and H. Pick[1], S. Amelinckx and E. Votava[2], and others. Here we report on figures obtained during evaporation experiments which recall similar figures obtained on the surface, for example, of silicon carbide by A. R. Verma[3] and on sodium chloride by Z. Morlin[4].

The annealing of the sodium chloride plates (15 mm. × 5 mm. × 2 mm.) was carried out near the melting point for 4–5 days in a crucible made from sodium chloride single-crystal and covered with a single-crystal plate. Besides the simple-concentric circles seen in Fig. 1 (the small spots on the figure are etch-pits revealed by glacial acid), figures of sharp characteristic contours were obtained (Fig. 2). These may represent Frank–Read sources, which appear at the edges of the sodium chloride plates,

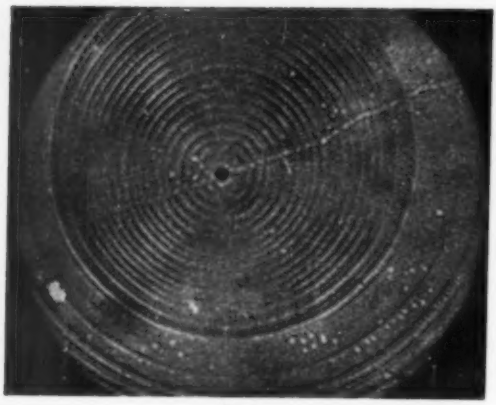

Fig. 1

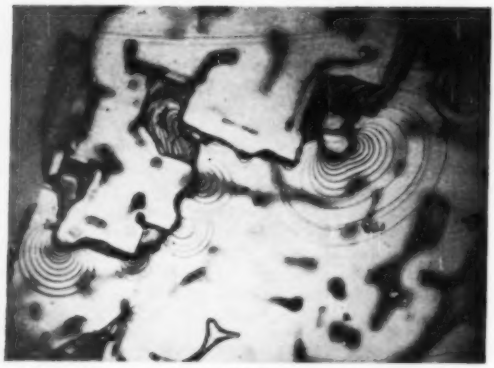

Fig. 2

especially on the edge of the surface where the two sodium chloride plates lay on each other during the evaporation.

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Exo-electron Emission and the Optical Properties of Oxide-coated Metal Surfaces

Evidence suggests that exo-electron emission from ionic crystals is associated with colour centres and kindred imperfections which result in energy-levels in the forbidden band of the crystal[1]. Grunberg and Wright[2] found very strong exo-electron emission from abraded aluminium, zinc and magnesium irradiated with light at 4700 Å. The tendency of these elements to form metal excess oxides led Grunberg and Wright to suggest that these may be present in the oxide oxygen ion vacancies occupied by two electrons called, by analogy with the alkali halides, F'-centres. The excitation of the F'-centres by light of 4700 Å. was suggested as an important process in the mechanism of exo-electron emission from metals.

The method of preparation of metal surfaces is known to affect the experimentally determined

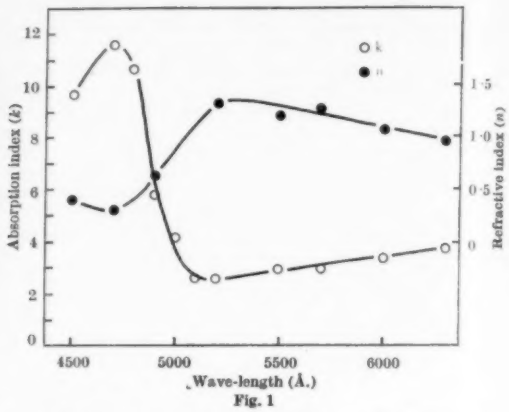

Fig. 1

optical constants, no doubt due to differences in structure of the surface layers. The oxide film on a mechanically polished metal surface would probably contain large numbers of the proposed F'-centres, which might be expected to increase the dielectric constant of the film in the region of 4700 Å. with a consequent alteration in the measured values of the optical constants.

The optical constants of mechanically polished aluminium and zinc have been measured for various wave-lengths in the visible region by the Drude method. Fig. 1 illustrates the variation in the absorption index, k, and the refractive index, n, for aluminium, showing a considerable increase and decrease, respectively, in the vicinity of 4700 Å. A similar result was obtained with zinc. Further work, at present in progress, is, however, required to establish a definite relationship with the proposed F'-centres.

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Ratio of Nucleon Mass and Electron Mass

With reference to the experimental value 1840 for the ratio of nucleon and electron mass, mentioned by Prof. A. J. Rutgers in *Nature* of September 19, p. 1959, it may be noted that the ratio of proton mass and electron mass is given by the exponential equation :

$$\frac{m_p}{m_e} = \frac{1}{2}\exp(-1) \times 10^4 = 1839{\cdot}39$$

More generally, the rest mass of an elementary particle, relative to the rest mass of the electron, is $m/m_e = k\exp(-x)$, and since $\exp(-x)$ is a 'die-away factor', this formula represents the tendency of the mass of an elementary particle to decrease. For all elementary particles except the electron with minimum rest mass, and the proton with relative rest mass $m_p/m_e = k\exp(-1)$, the tendency to decrease of rest mass has been demonstrated experimentally.

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Observation of Dislocations in Non-metallic Layer Structures

TRANSMISSION electron microscopy of thin foils, as developed by Hirsch, Whelan and co-workers[1], has become an important tool in studying the static[1,2] and kinetic[3] behaviour of dislocations in metals. Very few observations on non-metals have been published as yet. We have applied this technique to a number of non-metallic layer structures. One has then the advantage that very thin cleavage flakes can easily be prepared and, moreover, that the main glide plane usually coincides with the cleavage plane. In such cases extensive dislocation patterns will appear in the plane of observation. In particular, we have studied in some detail the following substances: bismuth telluride and antimony telluride, graphite, muscovite and talc. A few examples of patterns observed are reproduced in Figs. 1–3.

The c-plane of Bi_2Te_3 and Sb_2Te_3 is a glide plane and cleavage plane at the same time. Extensive hexagonal grids can be observed in both substances; Fig. 1 gives an example observed in Bi_2Te_3; very similar patterns are observed in Sb_2Te_3. For both substances a dissociation into partials is to be expected since glide occurs between close-packed planes. However, in both substances the basal dislocations generally appear undissociated with the resolving power available with the standard Philips microscope. In Bi_2Te_3, there is an indication that they may be dissociated over a small distance. Extensive movement of dislocations in the c-plane, and in pyramidal glide planes, giving rise either to elimination of dislocations or to the formation of networks, has been observed. The driving force for this process is heating of the foil by the electron beam, and the resulting temperature gradients. Hexagonal networks were also found in the basal plane of muscovite. It was found that heating with the electron beam gave rise to the 'precipitation' of gases into small bubbles located on dislocations (Fig. 2).

In graphite and talc the dislocations are found to be split into partials. The phenomenon is especially striking in talc where the equilibrium separation turns out to be approximately equal to $0{\cdot}2\mu$, as can be judged from Fig. 3. This implies a very small stacking fault energy. This very low value of the stacking fault energy should be representative for a class of clay minerals; it may explain why stacking faults occur so frequently in these substances. Fig. 3 shows dislocation ribbons and networks containing contracted and extended nodes somewhat similar to those observed in face-centred metals[2].

The dislocations in talc and in related clay minerals are of particular interest since, as a consequence of the hexagonal ring structure of the planes between which glide takes place, dislocations, split into four or six partials, are to be considered, giving rise to typical features not found in the face-centred metals.

A more detailed account of these observations will be published elsewhere.

We are indebted to Mr. J. Goens, director of the Centre d'Etude de l'Energie Nucléaire, Mol, for per-

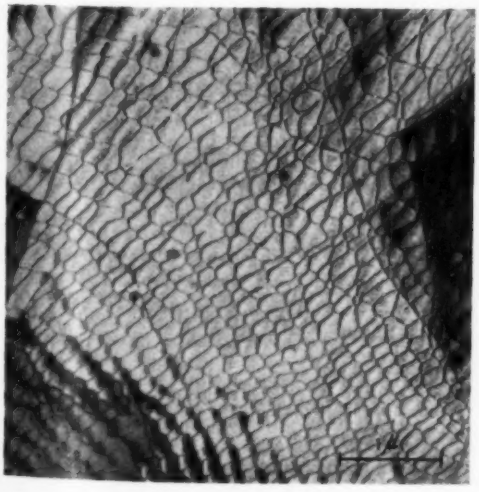

Fig. 1. Dislocation network in Bi_2Te_3. Note that certain segments of dislocations and certain node-points have left the foil

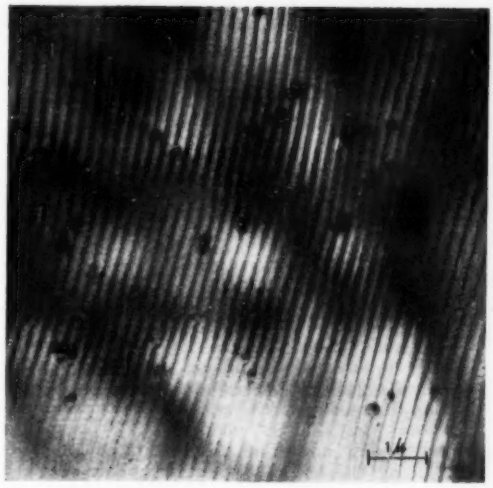

Fig. 2. Gas bubbles formed on dislocations in muscovite after irradiation with the electron beam

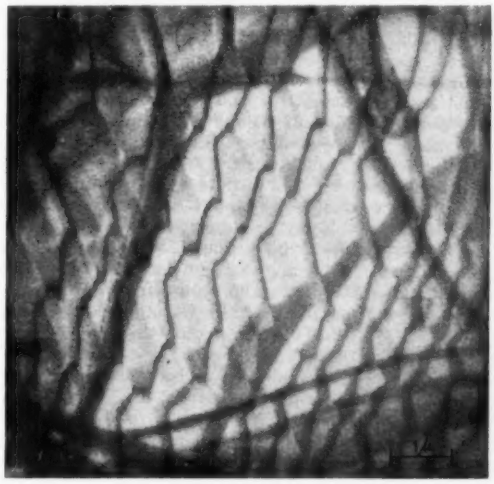

Fig. 3. Widely extended dislocations in the basal plane of talc. Note the formation of extended and contracted nodes

mission to publish this communication. We also wish to thank Mr. Nicasy for his skilful preparation of specimens and Mr. Beyens for the photographic work.

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CHEMISTRY

Two New Complex Calcium Ferrite Phases

The system $CaO–FeO–Fe_2O_3$ has been the subject of many investigations during the past decade, especially by Italian research workers studying the reduction of calcium ferrites and other ferrite phases of interest in cement chemistry. The phases $CaO.FeO.Fe_2O_3$ and $CaO.3FeO.Fe_2O_3$ have been identified by Burdese[1]. No ternary phases seem to have been observed in the sub-system hematite–dicalcium ferrite–magnetite. The purpose of this communication is to report the finding of two new ternary phases in this part of the system.

In a preliminary study of the systems Fe_2O_3–$CaFe_2O_4$–Fe_2O_4 and $CaFe_2O_4$–$Ca_2Fe_2O_5$–Fe_2O_4 several compositions were prepared within each triangle. Varying proportions of synthetic dicalcium ferrite, hematite and magnetite powders were mixed and small pellets were pressed. These were sealed in evacuated silica capsules, which were heated at 1,000° C. for 1–10 days and then quenched in water. The pellets were examined magnetically, microscopically, by X-rays, and analysed chemically. It soon became evident that two new ternary phases exist, located one in each of the composition triangles mentioned. The two phases appear to have the following approximate compositions: $3CaO.FeO.7Fe_2O_3$ located in the Fe_2O_3–$CaFe_2O_4$–Fe_2O_4 system and $4CaO.FeO.4Fe_2O_3$ in the $CaFe_2O_4$–$Ca_2Fe_2O_5$–Fe_2O_4 system. Samples having compositions close to these formulæ were non-magnetic and appeared mainly as single phases under a metallographic microscope. The stoichiometric compositions of the two new ternary phases are 24·0 per cent CaO, 7·7 per cent FeO and 68·3 per cent Fe_2O_3 for $4CaO.FeO.4Fe_2O_3$ and 12·4 per cent CaO, 5·3 per cent FeO and 82·3 per cent Fe_2O_3 for $3CaO.FeO.7Fe_2O_3$. Table 1 lists the *d*-spacings in Å. units and the relative intensities for the two phases as determined by a recording X-ray diffractometer.

The pattern of $3CaO.FeO.7Fe_2O_3$ is strikingly similar to that reported[2,3] for calcium diferrite ($CaO.2Fe_2O_3$), suggesting that this ternary phase may be a solid solution between magnetite and calcium diferrite in analogy with other limited solid solutions in the system $CaO–FeO–Fe_2O_3$. Phase relationships and other data for the system hematite–magnetite–dicalcium ferrite will be reported when the current study of the oxygen potential for this system has been completed.

Table 1

$4CaO.FeO.4Fe_2O_3$		$3CaO.FeO.7Fe_2O_3$	
d	I/I_0	*d*	I/I_0
11·3	25	15·7	20
5·6	35	5·2	10
3·74	10	4·9	25
2·99	30	3·11	20
2·81	100	2·97	40
2·67	15	2·92	15
2·52	15	2·67	40
2·49	15	2·62	35
2·29	20	2·58	100
2·24	15	2·54	30
2·06	20	2·15	20
1·84	15	1·99	15
1·73	15	1·84	15
1·58	10	1·70	20
1·50	10	1·56	20
		1·48	20

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Effect of High-Energy Radiation on Mixtures of Vinyl or Related Polymers with Unsaturated Compounds

A mechanism has been recently proposed[1] to account for the behaviour of polypropylene on irradiation, in which the formation of a cross-link between molecules involves reaction between an activated centre in the polymer and a chain fragment containing a vinylidene double bond. This suggests that the cross-linking induced by radiation would be enhanced by the incorporation of unsaturated additives into this polymer. Considerable enhancement of cross-linking has been claimed to occur in the irradiation of 'solid solutions' of polyvinyl chloride in di- and tri-allyl esters[2].

Consideration of the above prompted an investigation into the effect of unsaturated compounds on addition polymers in general and on polymers of the vinyl family in particular. Compounds chosen to represent three classes of unsaturation were diethyl maleate, dibutyl itaconate and triallyl cyanurate. To ensure that any enhancement would be detected, it was desirable to incorporate into the polymers as much additive as possible. However, for ease of interpretation, the concentration should lie within the range in which any reaction with the polymers could be regarded as the result of an indirect effect of the radiation on the additive. An additive concentration of 10 per cent was chosen as a reasonable compromise.

The preliminary results of this survey are presented in Table 1, the criterion for enhancement of cross-linking being the variation of sol fraction with dose for the polymer plus additive when compared with that of the polymer alone (in this table 'No' indicates

Table 1

Polymer	Enhancement of cross-linking in the presence of		
	Diethyl maleate	Dibutyl itaconate	Triallyl cyanurate
Polyethylene	None	None	Slight
Polypropylene	Slight	Slight	Good
Poly*iso*butylene	No	No	No
Polyvinyl alcohol	No	No	Good
Polyvinyl formal	Good	No	Good
Polyvinyl acetate	Slight	Slight	Good
Polyvinyl methyl ether	No	No	No
Polyvinyl chloride	Slight	No	Good
Polyvinyl pyrrolidone	No	No	Good
Polystyrene	No	No	Good
Polyvinyl carbazole	No	No	Good
Polymethyl acrylate	None	None	Slight
Polymethyl methacrylate	No	No	Good

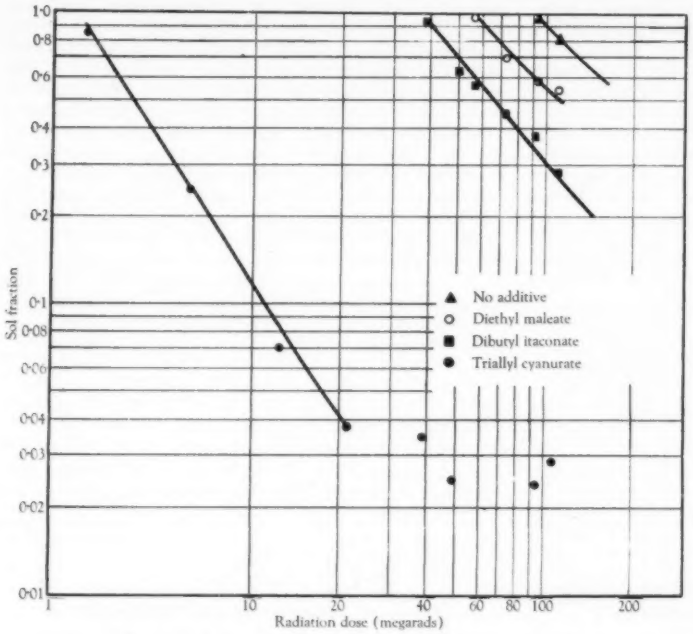

Fig. 1. Effect of unsaturated additives on polyvinyl acetate

that no gel fractions were obtained with or without the additive up to the highest dose used).

The superiority of triallyl cyanurate in enhancing cross-linking is believed to be due mainly to the presence of three unsaturated groups in the molecule. The much greater efficiency of triallyl esters compared with diallyl esters in polyvinyl chloride has already been noted[2].

Typical examples of the effect of these additives are shown in Figs. 1 and 2.

Fig. 1 shows the variation of sol fraction with dose for polyvinyl acetate alone and when mixed with the unsaturated compounds. The curves through the experimental values are drawn for degradation to cross-linking (β/α) ratios of 0·4 (polymer alone), 0·4 (polymer plus diethyl maleate), 0·2 (polymer plus dibutyl itaconate) and 0·0 (polymer plus triallyl cyanurate).

Fig. 2 similarly shows the variation of sol fraction with dose for polymethyl acrylate alone and when mixed with the additives. The curves are drawn for β/α ratios of 0·2 (polymer alone or mixed with diethyl maleate or dibutyl itaconate) and 0·0 (polymer plus triallyl cyanurate). While it is found that the addition of triallyl cyanurate to a polymer frequently gives a β/α ratio of 0·0 on irradiation, the other additives affected this ratio to a much smaller extent.

Poly*iso*butylene and polymethyl methacrylate are examples of polymers which have only a negligible tendency to develop cross-links under ionizing radiation. However, while mixtures of poly*iso*butylene with the additives became degraded, polymethyl methacrylate containing triallyl cyanurate gelled readily. This comparison suggests that the cross-linking of polymethyl methacrylate by triallyl cyanurate occurs through the ester groups. Comparison of energy yields for gas evolution and main-chain scission in polymethyl methacrylate indicates that each scission is accompanied by the decomposition of approximately one side-chain[3]. If it is assumed that addition of triallyl cyanurate results in each side-chain decomposition becoming converted to one cross-link, then the variation of sol fraction with dose would be expected to correspond with a β/α ratio of about 1. In fact, the variation of sol fraction with dose corresponds to β/α less than 0·4, so that it appears that the additive can interfere directly with main-chain scission unless, as has been tentatively suggested[3], main-chain scission arises as a direct result of side-chain scission in this polymer.

The results obtained with polypropylene are of interest in that the enhancement of cross-linking decreased with increase of the time between preparation of the sample and its irradiation. This may be due to the insolubility of the additive which immediately after compounding is present as a dispersion in the polymer, but on standing, diffuses to the surface, thus reducing the bulk concentration.

The frequent correspondence of the sol fraction–dose curves with the theoretical curves for a particular value of the β/α ratio suggests that graft polymerization of the additive is not the correct explanation of this enhancement of cross-linking. This conclusion is supported by the fact that one of the additives, diethyl maleate, has a marked reluctance to homo-

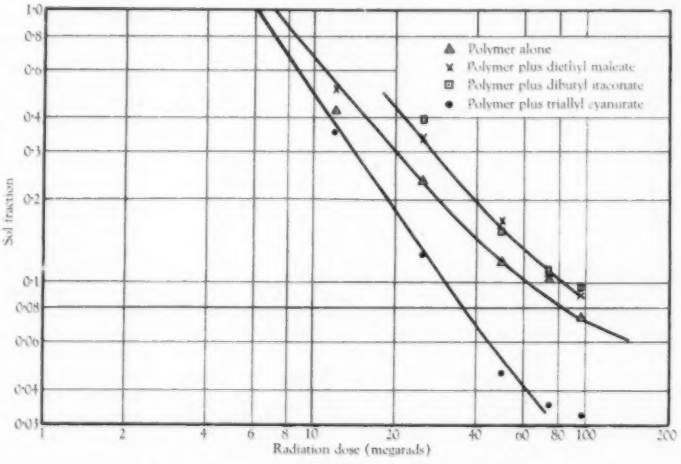

Fig. 2. Effect of unsaturated additives on polymethyl acrylate

polymerize and by the low rate at which such a polymerization would occur with the other additives at the concentration used and in such viscous media.

The additives, particularly triallyl cyanurate, seem to operate either by inhibiting chain scission in these polymers or by converting chain scission into a cross-linking reaction. It is possible that these additives may react with all the primary products of the action of ionizing radiation on the polymer. Examination of the effect of hydrolysis on the gel fraction of triallyl cyanurate cross-linked polymers may indicate the nature and extent of the interaction.

It is hoped to report the results of this investigation more fully at a later stage.

My thanks are due to Dr. R. M. Black for his advice and encouragement and to Dr. L. G. Brazier, director of research, British Insulated Callender's Cables, Ltd., for permission to publish this communication.

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Second Explosion Limit of Dried Carbon Monoxide–Oxygen Mixtures

The position of the second explosion limit of carefully dried mixtures of carbon monoxide and oxygen in quartz vessels has been determined. Both the heating and withdrawal methods were used in a static system. Carbon monoxide was prepared from sodium formate and concentrated sulphuric acid, and oxygen by heating potassium permanganate. After being passed through chemical desiccants and then through cold traps, the gases underwent a final drying operation immediately before use. This final drying consisted in allowing the gases (sometimes premixed) to stand in 'Pyrex' drying vessels surrounded by liquid oxygen for at least 12 hr.

Explosion limits for carbon monoxide – oxygen (1 : 2) mixtures in the pressure-range 40–250 mm. mercury lay between the temperatures 750° and 840° C., and are shown in Fig. 1 together with the published results of other workers. It will be seen that the present results lie at considerably higher temperatures than so far reported. Experiments were also made using gas mixtures which had not undergone the *final* drying procedure mentioned above. The limits were found to lie at a temperature some 100° C. lower. Gordon and Knipe[1] have shown that small traces of water vapour lower considerably the limit temperature. We suggest, therefore, that the higher limits reported here can be attributed to the use of drier gases than those employed in earlier work.

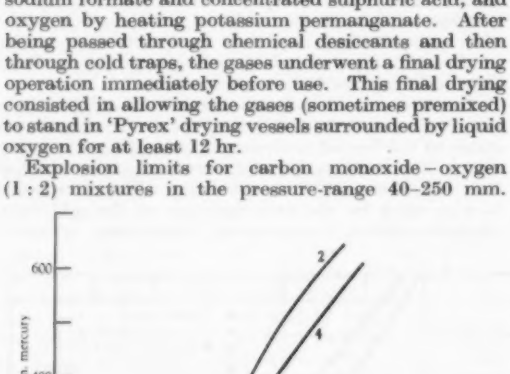

Fig. 1. Position of second explosion limit in the dry carbon monoxide – oxygen reaction
(1) Knipe and Gordon (ref. 1), ($2O_2$: CO); (2) Hadman, Thompson and Hinshelwood (ref. 2), ($2O_2$: CO); (3) Hoare and Walsh (ref. 3), ($2CO : O_2$); (4) Lewis, von Elbe and Roth (ref. 4), ($2O_2$: CO); (5) present work ($2O_2$: CO); (6) present work with the final drying process omitted

A detailed report of this and related work, including an account of the effects of mixture composition and of added inert gases, will be published elsewhere.

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New Approach to the Synthesis of O-Phosphoserine and Related Peptides

A general method of synthesizing phosphorylated amino-hydroxy acids and derived peptides, using diphenylphosphorylchloridate as the phosphorylating agent, was introduced by Riley *et al.*[1]. This method has been applied with rather satisfactory results in the synthesis of α-carbethoxy-L-lysyl-L-(O-phosphoryl)-serylglycine[2]; but further studies on the inhibitory spectrum of phosphoserine[3] towards proteolytic enzymes, and the effect of phosphatases[3] upon various substrates as well, stress the necessity of alternate synthetic methods.

When diphenyl groups from O-diphenylphosphoryl peptide derivatives containing other than aliphatic side-chain amino-acids are removed by catalytic hydrogenation in the presence of platinum catalyst, the likelihood of reduction of the side-chain rings is apparent. In this connexion it is of interest to note that O-diphenylphosphoryl esters have been believed up to the present to resist hydrogenolysis in the presence of palladium catalyst. Based on this assumption, a stepwise removal of protecting groups from carbobenzoxy-D,L-(O-diphenylphosphoryl)serine benzyl ester has been recently reported[4]. This consists, first, in the removal of the carbobenzoxy and benzyl groups by hydrolysis in the presence of palladium and then of the phenyl groups using platinum catalyst. Thus, the intermediate product D,L-(O-diphenylphosphoryl)serine[4] was described as a crystalline compound with melting point 129–130°.

Our experience, however, with hydrogenolysis of O-diphenylphosphoryl serine peptide derivatives in the presence of palladium has led us to a different conclusion. Special emphasis has been placed so far on the hydrolysis of carbobenzoxy-D,L-(O-diphenylphosphoryl)serine benzyl ester. When the latter was hydrogenated in the presence of a palladium catalyst and two equivalents of hydrogen were absorbed in about 1 hr., we were unable to isolate the reported product O-diphenylphosphoryl serine[4].

Surprisingly enough, the oily product obtained, which is soluble in water, was proved by paper chromatography to be a mixture of at least three components. The major product consisted of monophenylphosphorylserine[5], while two other unknown compounds were travelling with entirely different R_F value than that reported[4] for O-diphenylphosphorylserine.

Though the elucidation of this finding is still in progress, it is tempting to speculate that the emergence of the carboxyl- or amino-group of serine during the hydrolysis influences the elimination of a phenyl group via the formation of an intermediate six- or five-membered ring.

Unexpected difficulties were encountered also when diphenylphosphoryl chloridate was used to phosphorylate α-carbethoxy-(ε-carbobenzoxy)-L-lysylglycyl-L-serine benzyl ester. The latter peptide derivative was synthesized as follows: Tritylglycine[6] was coupled with serine benzyl ester by the carbodiimide method, and the thick oily product thus obtained was further detritylated to give glycyl-L-serine benzyl ester hydrochloride (I) in 75 per cent yield, melting point 173–175° (decomp., softens at 165–166°). Analysis: calc., $C_{13}H_{17}N_3O_4Cl$, N 9·70, Cl 12·28; found, N 9·50, Cl 11·90.

Compound I was coupled with α-carbethoxy-(ε-carbobenzoxy)-L-lysine[2] as previously described. In our experience and in spite of a previous statement[7], coupling in anhydrous solution leads to a considerable extent to the formation of the O-peptide isomer, which is difficult to remove.

The tripeptide derivative obtained, α-carbethoxy-(ε-carbobenzoxy)-L-lysylglycyl-L-serine benzyl ester (II), melted at 141–142° (sharp), yield 40–45 per cent, $[\alpha]_D^{25}$ 7·4 (c. 0·54 in glacial acetic acid). Analysis: calc., $C_{29}H_{32}N_4O_8$, C 59·36, H 6·52, N 9·7; found, C 59·45, H 6·72, N 9·53.

Compound II was phosphorylated with diphenylphosphorylchloridate in a similar manner to that described for its analogue, α-carbethoxy-(ε-carbobenzoxy)-L-lysyl-L-serylglycine benzyl ester[2]. Several attempts to obtain the product in a solid form have failed, probably owing to the presence of unphosphorylated peptide derivative which is difficult to separate by fractional precipitations. When a larger excess of chloride was used the result turned out to be less satisfactory. The oily product obtained, when hydrogenated and studied by paper chromatography, was found to give a mixture of several ninhydrin-positive spots. The possibility of some splitting of peptide bonds was naturally borne in mind[8].

In the course of our studies for improved methods for the synthesis of O-phosphorylated peptides, we have employed di-*p*-nitrobenzylphosphorylchloridate[9] as the phosphorylating agent.

Since benzyl groups are split off by catalytic hydrogenation with palladium catalyst, this method may be of wider application than that employing diphenylphosphorylchloridate.

Moreover, di-*p*-nitrobenzylphosphorylchloridate was expected to give readily crystallizing products as in the case of N-phosphoryl amino-acids and peptides[10]. Indeed, we have succeeded in preparing carbobenzoxy-D,L-(O-di-*p*-nitrobenzylphosphoro)-serine benzyl ester in crystalline form in 50–60 per cent yield. The product was melted at 107–108°, while the corresponding diphenylphosphoryl derivative has a considerably lower melting point (49–50°) and is difficult to crystallize. Analysis: calc., $C_{32}H_{30}N_3O_{12}P$, N 6·1, P 4·57; found, N 6·2, P 4·85.

Tetra-*p*-nitrobenzylpyrophosphate, readily prepared from di-*p*-nitrobenzylphosphate and carbodiimide in dimethylformamide, constitutes another route under investigation. So far we have succeeded in phosphorylating α-amino groups in the presence of tertiary base. Thus, N-di-*p*-nitrobenzylphosphoroglycine benzyl ester was prepared in about 50 per cent yield, melting point 111–112°. Analysis: calc., $C_{33}H_{32}N_3O_{13}P$; N 8·15, P 6·09; found, N 8·05, P 6·32.

The potentialities of di-*p*-nitrobenzylphosphorylchloridate and tetra-*p*-nitrobenzylpyrophosphate for the synthesis of O-phosphorylated peptides will be discussed elsewhere.

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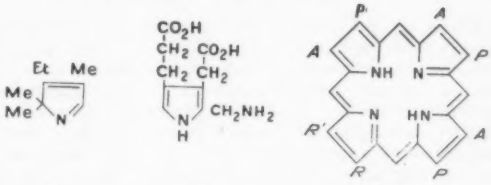
Formation of I- and III-Type Porphyrins by the Polymerization of Pyrroles

In a recent paper[1] we discussed the alkylation of tri- and tetra-alkylpyrroles and referred to the 2 : 3 : 4-trialkylpyrroles which on alkylation could give either 2 : 3 : 4 : 5-tetra-alkylpyrroles or 2 : 2 : 3 : 4-tetra-alkyl-2(H)pyrroles (for example, I). The factors which decided the course of this reaction were delicately balanced, for whereas the methylation of the Grignard derivative of 2 : 3 : 4-trimethylpyrrole gave 2 : 3 : 4 : 5-tetramethylpyrrole almost exclusively, a similar methylation of 2 : 4-dimethyl-3-ethylpyrrole (cryptopyrrole) gave 3-ethyl-2 : 2 : 4-trimethyl-2(H)pyrrole (I) as the major product.



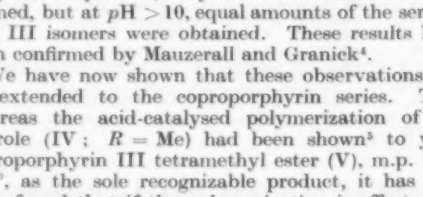
(I) (II) (III)

$A = \cdot CH_2 \cdot CO_2H$
$P = \cdot CH_2 \cdot CH_2 \cdot CO_2H$

This duality of reaction path has some interesting consequences, in particular in considering the biogenesis of natural porphyrins which are derived by the polymerization of porphobilinogen (II). Most of the common porphyrins belong to the so-called III series, for example, uroporphyrin III (III; $R = P$, $R' = A$). Although members of the I series, for example uroporphyrin I (III; $R = A$, $R' = P$), are also natural products, the II and IV series apparently do not occur naturally. In considering the mechanism

by which the I- and more especially the III-type porphyrins might be formed from porphobilinogen it is clear that the initial reaction is the electrophilic alkylation of one molecule of porphobilinogen, a 2 : 3 : 4-trialkylpyrrole, by another porphobilinogen molecule. We have suggested[2] that, if this occurs at the 5-position, as in the methylation of 2 : 3 : 4-trimethylpyrrole, in a repeating process then uroporphyrin I will be the eventual product ; if reaction occurs at the 2-position as in the methylation of cryptopyrrole, then uroporphyrin III results after a series of specified migrations. It was therefore of interest to ascertain how far this type of polymerization could be controlled to give porphyrins of the I or III series. Such reactions have considerable biochemical as well as chemical interest as certain porphyrias are known to be associated with the biological production of I- rather than III-type porphyrins. Cookson and Rimington[3] examined the polymerization of porphobilinogen under various conditions *in vitro* and found that, at 100°, uroporphyrin III was obtained rapidly and in high yield with no trace of the series I isomer. At 20°, the polymerization took several days and was dependent on *p*H ; at *p*H 6·5, only the series III isomer was formed, but at *p*H > 10, equal amounts of the series I and III isomers were obtained. These results have been confirmed by Mauzerall and Granick[4].

We have now shown that these observations can be extended to the coproporphyrin series. Thus whereas the acid-catalysed polymerization of the pyrrole (IV ; R = Me) had been shown[5] to yield coproporphyrin III tetramethyl ester (V), m.p. 151–154°, as the sole recognizable product, it has now been found that if the polymerization is effected by hot ethanolic ammonia, the product is mainly coproporphyrin I tetramethyl ester, m.p. 237–240°, containing some of the series III isomer.

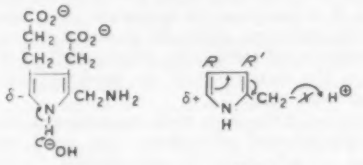


(IV) (V)

(P_{Me} = $-CH_2\cdot CH_2\cdot CO_2Me$)

Likewise, polymerization of the corresponding dicarboxylic acid (IV ; R = H) in ethylene glycol solution in presence of sodium carbonate, gave a product which, after esterification by methanolic hydrogen chloride, could be resolved by chromatography into fractions which were mainly coproporphyrin I tetramethyl ester on one hand and mainly the series III isomer on the other. These identifications were made on the basis of melting points of the methyl esters and chromatographic examination of the free porphyrins in the system 2 : 6-lutidine–water, and we are very grateful to Prof. C. Rimington and Mrs. A. Latter, who carried out these determinations.

The course of these *in vitro* polymerizations is therefore controlled by *p*H, a high *p*H leading to the formation of a mixture of I- and III-type porphyrins and a low *p*H leading only to the III-type. From the mechanistic point of view, the alkaline polymerization is regarded as involving a loosening of the pyrrole N–H bond by the alkali, leading to an increased electron density in the pyrrole ring (as in VI). This enhances the ease of electrophilic substitution at the vacant 5-position and leads eventually to I-type porphyrins. Ionization of the side-chain carboxyl groups in porphobilinogen will doubtless accentuate this effect, but the parallel results with the pyrrole esters (for example, IV) show that the free acid groups are not essential.



(VI) (VII)

In acidic media, a pyrrole of type (VII) will tend to ionize in the manner shown (X = OAc, Br or $\overset{+}{N}H_3$ in the protonated form of porphobilinogen), which causes a deactivation of the ring towards electrophilic attack of the 5-position and thus favours reaction at position 2-. This substitution pattern leads to the formation of III-type porphyrins. It is not yet clear how far these ideas can be extended to the *in vivo* polymerizations of porphobilinogen to uroporphyrins I and III, but it would appear probable that certain aspects of the reaction mechanisms are common to both *in vivo* and *in vitro* porphyrin syntheses. These views were communicated to Prof. A. Neuberger, who included them in his Section Lecture to the Seventeenth International Congress of Pure and Applied Chemistry at Munich, 1959.

In recent papers, Bogorad[7] describes the isolation of an enzyme, porphobilinogen deaminase, which causes the polymerization of porphobilinogen to uroporphyrinogen I (cf. alkaline catalysis), but in the presence of a second enzyme, uroporphyrinogen isomerase, the product was uroporphyrinogen III (cf. acid catalysis). It is possible that some chemical interaction occurs between the two enzymes which causes a modification of the essential functional groupings, and it may not be necessary to postulate, as Bogorad does, a substrate other then porphobilinogen for the isomerase.

In order to meet Bogorad's suggestions, Wittenberg has recently[8] published a mechanism for porphobilinogen polymerization which involves an octapyrrolic intermediate with successive dehydrogenation and hydrogenation steps. Apart from the improbability that a 24-membered macrocylic ring would be formed in such a facile reaction, the theory does not offer a convincing explanation of the exclusive production of III-type porphyrins under conditions involving acid catalysis. Moreover, it postulates for the formation of the tripyrromethane portions of the large macrocycle a type of condensation which has not been observed in the laboratory.

Wittenberg also refers to the problem of the biogenesis of vitamin B_{12} which, like the porphyrins, has porphobilinogen as a pyrrolic intermediate. He makes the point that if the formation of the linkage between rings *A* and *D* is the initial step in the polymerization, as we suggest, this does not accord with the view we have previously advanced[9], that the final ring closure in the formation of vitamin B_{12} is the formation of the direct link between rings *A* and *D*. These apparently contradictory views can be reconciled if an additional rearrangement of

uroporphyrinogen III is involved. The nature of this reaction is unknown but a pinacol rearrangement of the type visualized by Woodward[10] to explain the exocyclic C_1 substituent in magnamycin is a possibility and is being examined in our laboratory.

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BIOCHEMISTRY

Free Amino-acids of Some Fungi

The nature and amounts of free amino-acids in higher plants are becoming relatively well known since the advent of paper chromatography. However, few investigations of amino-acids in the Cryptogams have been made. Fowden[1] has studied the amino-acids of certain algae, Mansford and Raper[2] those of *Mucor mucedo*, Fluck and Richle[3] those of *Fusarium lycopersici*. The yeasts, *Aspergillus*, *Penicillium* and *Neurospora* species[4], have been extensively studied but the rest of the fungi remain largely unexamined.

Robbins[5] has classified fungi physiologically according to their ability to utilize various forms of nitrogen: Group I, Molecular nitrogen, NO_3^-, NH_4^+ and organic nitrogen; Group II, NO_2^-, NH_4^+ and organic nitrogen; Group III, NH_4^+ and organic nitrogen; Group IV, organic nitrogen.

It appeared desirable to study the free amino-acids of a taxonomic range of fungi which included most of these physiological groups. The species chosen were as follows: Phycomycetes—*Pythium ultimum* Trow. (Group II); *Phytophthora cactorum* Leb. and Cohn (Schroet.) (Group IV); *Phycomyces nitens* + (Agardh) Kunze and Schmidt (Group IV); *Thamnidium elegans* Link (Group III). Ascomycetes and Fungi Imperfecti—*Chromocrea spinulosa* (Fuckel) Petch (Group II); *Fusarium culmorum* (W.G.Sm.) Sacc. (Group II); *Fusarium javanicum* Koorders (Group II). Basidiomycetes—*Stereum purpureum* Pers. ex Fries (Group II).

Pythium ultimum was cultured on liquid Czapek–Dox medium with nitrate as the nitrogen source and sucrose as the carbon source. The others were grown on a liquid medium in which asparagine (0·3 per cent) was the nitrogen source and glucose (2 per cent) the carbon source. Minerals and vitamins included potassium dihydrogen phosphate (0·1 per cent), magnesium sulphate and potassium chloride (0·05 per cent) and trace amounts of Ca^{++}, Fe^{++}, Zn^{++}, Cu^{++}, Mn^{++}, MoO_4^- and thiamine. All fungi were grown at 25° C. as stationary cultures in 250 ml. Erlenmeyer flasks containing 100 ml. liquid medium.

After varying intervals of time depending on the species growth-rate, fully developed mycelial pads still in growth were separated from the medium and were washed once with distilled water. The amino-acids were then extracted by blending the hyphæ with 87 per cent alcohol at room temperature. The extracts were concentrated and then examined for amino-acids by paper chromatography.

A summary of the free amino-acids found in the fungal hyphæ is presented in Table 1.

Several amino-acids were found in all the fungi studied. Fowden[1] found a similar pattern in three species of algae. The amino-acid, γ-amino butyric, has been found in a wide range of plants and it is interesting to record its presence in seven of the eight fungi examined. It is not a constituent of protein hydrolysates, nor is β-alanine, which was found in four of the fungi. Large amounts of proline

Table 1. Free Amino-acids Present in the Hyphal Extract of Certain Fungi

	Pythium ultimum (on Dox)	*Phytophthora cactorum*	*Phycomyces nitens* +	*Thamnidium elegans*	*Chromocrea spinulosa*	*Fusarium culmorum*	*Fusarium javanicum*	*Stereum purpureum*
Aspartic acid	++	++	+++	+++	++	+++	+++	+++
Glutamic acid	++	+++	+++	+++	+++	+++	+++	+++
α-Alanine	+++	+++	+++	+++	+++	+++	+++	+++
β-Alanine	−	++	+	+	−	−	+	−
γ-Amino butyric acid	++	+++	++	++	+++	++	+	−
Serine	+	++	++	+	++	+++	++	++
Glycine	++	++	++	+	++	++	++	+
Threonine	++	++	++	−	+	+	++	+
Proline	−	+++	−	++	−	−	−	−
Tyrosine	−	+	+	−	+	−	+	−
Arginine	+++	+++	+++	+	++	++	++	++
Histidine	++	++	++	+	++	++	++	++
Lysine	++	++	−	−	++	−	++	++
Phenylalanine	−	−	+	+	+	−	−	−
Leucine and/or *iso*-leucine	++	++	++	+	++	++	++	+
Methionine and/or valine	++	++	++	+	+++	++	++	+
Ornithine	−	+	−	−	−	+	−	+
Cysteic acid	++	+	−	+	++	++	+	−
Asparagine	++	+++	+++	+++	+++	++	+++	+++
Glutamine	+++	+++	+++	+++	+++	+++	+++	+++
Initial *p*H	3·7	4·2	4·2	4·2	4·2	4·2	4·2	4·2
Final *p*H	5·5	4·7	6·7	3·9	5·1	7·0	6·9	6·5
Incubation time (days)	10	29	16	26	14	14	24	19

+++, Strong ninhydrin colour; ++, moderate colour; +, weak colour; −, not detected.

were found in *Phytophthora cactorum* and its presence was noted in *Thamnidium elegans*. Tyrosine was present in small amount in several, but tryptophan was not detected in any of the fungi. Glutamine appeared to be present in larger amounts than asparagine. Four unidentified compounds were found in some of the fungi. These corresponded on chromatograms to the positions of α-amino adipic acid, 3 : 4-dihydroxyphenylalanine, ethanolamine and taurine, but identification must await further work.

Under these experimental conditions, there do not appear to be any substantial differences between fungi belonging to different taxonomic and physiological groups. The number and relative amounts of free amino-acids present in fungi show an overall similarity to those in higher plants.

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Specificity *in vitro* of a Phenoloxidase System from *Periplaneta americana* (L.)

Enzymes capable of oxidizing mono- and diphenols are widely distributed in insects; some of these compounds are involved in the biosynthesis of exoskeletal substances, notably sclerotin[1]. While several *ortho*- and *para*-diphenols have been extracted from cuticle, relatively little is known about the corresponding synthetic enzymes. Recent work in connexion with the reaction of phenolic derivatives with proteins ('tanning reaction') has been reviewed by Hackman[2], Mason[3] and Dennell[4]. The present results form part of an investigation of the intermediary metabolism of phenolic substrates involved in sclerotin formation in *Periplaneta*.

It has been already shown that the sclerotin walls of the egg capsule (ootheca) are formed by the intermingling of the secretions of the left and right colleterial glands[1]. As a result of this, protocatechuic acid[5] (3 : 4-dihydroxybenzoic acid) is liberated from its 4-O-β-D-glucoside (secreted by the left gland) by the action of a β-glucosidase (from the right gland)[6]. Some evidence[1] suggests that the protocatechuic acid is oxidized enzymically by a secretion of the left gland[7], afterwards to link with structural proteins to form sclerotin.

It has now been confirmed that the oxidative enzymes are present in the lumen of the left gland and are released in the form of a highly turbid suspension when the dissected left gland is allowed to stand for a few minutes in distilled water. The preparation can be freed from cellular debris by centrifugation at 0° C. and from endogenous substrates by dialysis ('Cellophane') against 0·01 *M* sodium chloride. Subsequent salt precipitation gave fractions of very high enzymic activity between 0·1 *M* and 0·2 *M* sodium chloride (final concentration).

The activity of the dialysed enzyme preparations was investigated in 0·1 *M* sodium phosphate buffer (*p*H 6·8) with a variety of phenolic compounds (each in a final concentration of 0·002 *M*) using Warburg manometers (5–6 ml.) at 37° in an atmosphere of oxygen. The results are shown in Table 1.

Table 1. Substrates for the Phenoloxidase System from Left Colleterial Glands of *Periplaneta*

Active	Inactive
Protocatechuic acid	DL-3 4-Dihydroxyphenylalanine
3 : 4-Dihydroxybenzoic acid	L-Tyrosine (*para*)
3 : 4-Dihydroxypropionic acid	L-Tyrosine (*ortho*)
3 : 4-Dihydroxybenzaldehyde	*p*-Hydroxybenzoic acid
Catechol	DL-3 : 4-Dihydroxyphenylethylamine (dopamine)
Hydroquinone	Resorcinol
p-Phenylenediamine	

The enzyme promoted rapid oxidation of a number of *o*- and *p*-diphenols with the notable exception of 3 : 4-dihydroxyphenylalanine and the corresponding amine. L-Tyrosine (either *ortho* or *para*) or other monophenols were not oxidized.

Thus, in the sense of Keilin and Mann[8] and Dawson and Tarpley[9], this enzyme can be regarded as a laccase and in no sense a tyrosinase.

The enzyme activity is abolished by being heated above 70° and by 0·002 *M* potassium cyanide. It is unaffected by 4-chlororesorcinol and diethyldithiocarbamate. Preliminary investigations indicate that the enzyme is a protein–copper complex.

It is emphasized that the enzyme preparation has not yet been obtained in a soluble form but that it occurs in the gland in a finely divided state exhibiting a strong Tyndall effect. This is supported by electron microscopy[10].

It has not yet been found possible to separate the enzyme from the protein-precursor of sclerotin, of which indeed the enzyme may be a part.

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Infra-red Spectra of Capsular Polysaccharides from Thirteen Strains of *Cryptococcus neoformans*

Studies of infra-red absorption spectra of immunopolysaccharides have received little attention until recently. Thus, Levine, Stevenson and Kabler[1] were able to show that the serologically reactive and type specific pneumococcal polysaccharides have distinctive spectra by which they can be identified. Later, Watson, Marinetti and Scherp[2] working with the specific hapten of group *C* meningococcus were successful in assigning a provisional structure for the hapten by the aid of infra-red spectral analysis. Inasmuch as purified cryptococcal polysaccharides have shown serological reactivity by precipitation

Table 1. INFRA-RED SPECTRAL DATA OF *C. neoformans* POLYSACCHARIDES

Sample*	Absorbance						Source
	5·77μ	6·24μ	6·85μ†	7·07μ	7·27μ†	8·0–8·2μ	
BRI-C	0·275	0·241	0·242	0·271	0·254	0·334	Human *CSF*‡
3723-*C*	0·358	0·410	0·405	0·454	0·418	0·487	Bovine mastitis
RE-C	0·392	0·425	0·425	0·463	0·446	0·512	Human *CSF*
2700-*C*	0·472	0·492	0·495	0·541	0·509	0·604	Pigeon environs
3717-*C*	0·449	0·455	0·452	0·505	0·468	0·561	Soil
3727-*C*	0·380	0·496	0·445	0·530	0·495	0·525	Bovine mastitis
2400-*C*	0·498	0·535	0·585	0·640	0·598	0·649	Human bone
2600-*C*	0·234	0·283	0·435	0·330	0·354	0·344	Pigeon environs
MY-C	0·495	0·488	0·438	0·560	0·526	0·621	Human *CSF*
BRI-P	0·425	0·421	0·516	0·470	0·519	0·501	Human *CSF*
3723-*P*	0·310	0·362	0·553	0·399	0·493	0·402	Bovine mastitis
DU-P	0·265	0·275	0·364	0·310	0·354	0·332	Human bone
TRE-P	0·349	0·365	0·505	0·410	0·486	0·435	Human *CSF*
HU-P	0·302	0·323	0·445	0·374	0·426	0·402	Human *CSF*
BYR-P	0·330	0·330	0·625	0·380	0·576	0·370	Human *CSF*

* Sample: *C*, crude preparation; *P*, pure (capable of stimulating antibody formation in mice).
† Corrected for 'Nujol' absorption.
‡ *CSF*, Cerebrospinal fluid.

with specific hyperimmune rabbit serum[3,4] in addition to stimulating antibody formation in mice[5], it was deemed desirable to investigate their infra-red spectra and to compare these with the spectra of crude preparations.

Samples of the polysaccharides from pathogenic *Cryptococcus neoformans* strains were purified by the methods of Gadebusch[5], triturated in repurified commercial paraffin oil ('Nujol'), and spectra obtained from a paste thickness of approximately 0·01 mm. by means of a Perkin–Elmer double-beam recording spectrophotometer. In all cases the thinnest film possible was employed to bring out detail between 8·5 and 15μ. Crude polysaccharides were so designated because they had not been specifically deproteinized by the methods of Sevag[6].

In spite of the diverse origin of the cryptococcal polysaccharides (Table 1), the spectra were so strikingly similar that identification seems extremely difficult, if not impossible. Purification of these substances, while producing definite immunological differences[5], did not alter their infra-red spectra beyond a somewhat greater resolution of existing peaks. These spectral relationships have been borne out by analytical data which have shown similar values for carbon, hydrogen, oxygen, reducing sugar, uronic acid and acetyl groups (unpublished work). All these polysaccharides contain negligible amounts of nitrogen and phosphorus.

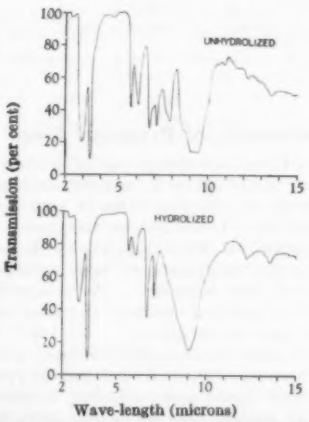

Fig. 1. Infra-red spectra of hydrolysed and unhydrolysed purified polysaccharide from *C. neoformans* strain *BRI*

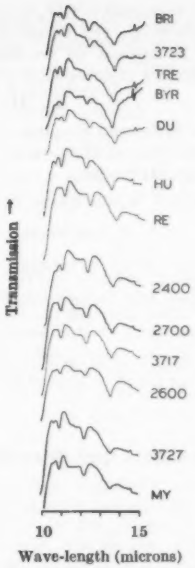

Fig. 2. Infra-red spectra of *C. neoformans* polysaccharides. The upper six spectra were from purified samples and the remainder were from crude preparations

As a result, it seems quite unlikely that capsular type identification as performed serologically by Evans[7] could be accomplished by a study of the infra-red spectra of their polysaccharides. In this respect at least spectral investigations of pneumococcal polysaccharides have been more encouraging[8].

Despite partial interference by 'Nujol' absorption (3·43μ, 6·85μ, 7·27μ), a few preliminary remarks may be made regarding the infra-red spectra of *C. neoformans* polysaccharides: (1) The source for the moderately strong carbonyl band at 5·77μ is probably the ester linkage and more specifically O-acetyl. Acids absorbing at this wave-length have been eliminated as a source, since precipitation was not carried out at low *p*H. In addition, the presence of the frequently accompanying 8·0–8·2μ band lends further confirmation to the ester origin. (2) Bands at 6·20 and 7·10μ are characteristic of the carboxylate ion which in turn may be derived from uronic acids. Since these polysaccharides all contain a uronate moiety, the bands at 6·24 and 7·07μ may well have been displaced somewhat. (3) Although bands at 6·85 and 7·27μ are partially attributable to 'Nujol' absorption, the intensity of absorption indicates the presence of another structural component, probably the $-CH_3$ group. (4) Carefully controlled hydrolysis of a water solution of *C. neoformans* strain *BRI* purified polysaccharide in the presence of sodium hydroxide produced a substantial diminution in the absorption spectra at 5·77, 6·24, 7·07, and 7·27μ (Fig. 1). The band at 8·0–8·2μ now appears only as a shoulder on the larger, broader band between 9 and 10μ. These changes have been interpreted as a combination of ester and uronate hydrolysis. The moderate decrease in absorption of the 7·27μ band indicates

partial loss of this terminal —CH_2 group. (5) Finally, in the region above 8·5μ, the bands at 11·15, 12·50 and 13·85μ (Fig. 2) appear to be characteristic for both crude and purified cryptococcal polysaccharides.

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Carnitine in Lipid Metabolism

The finding by Fraenkel and Friedman[1] that carnitine (4-trimethyl amino 3 hydroxy butyric acid) is an essential growth factor for certain organisms (vitamin B_T) and its availability by synthesis have renewed interest in the problem of its biochemical function.

Recent reports suggest that carnitine is implicated in lipid metabolism. Schaepdryver and Vleeschhouwer[2] showed that it increased the fat content of lymph; Fritz and McEwan[3] postulated a role in fat transport; and it has been reported present in vagotonin[4] and lipocaic[5]. Binon and Deltour[6] reported that, contrary to the belief that the nitrogenous base of dog serum phospholipid was all choline, one-third was actually carnitine.

The chemical similarity of carnitine and choline suggests that carnitine might possess anti-lipotropic activity. This possibility was examined by the 6-day mouse test of Welch and Welch[7]. Seventy young male mice were fed on (*a*) high fat, negative control diet; (*b*) positive controls containing 0·5 per cent choline; (*c*) test diet containing 0·5 per cent carnitine; and (*d*) test diet containing 1·0 per cent carnitine. The results (Table 1) show that carnitine had no effect on the fat content of the liver. This result substantiates the finding of Fritz[8] on rats.

As a further examination of the role of carnitine in lipid metabolism the finding of Binon and Deltour[6] was investigated. These authors analysed the total lipid fraction from dog serum by differential reineckate precipitation[9]. The precipitate at *p*H 10 was assumed to be choline, and that at *p*H 2, carnitine. The carnitine was not further identified.

Table 1. Total Lipid Content of Mouse Livers (Four Animals Grouped in Each Determination)

Group	High diet fat. Negative controls (choline + carnitine absent) (gm./100 gm.)	Plus 0·5 per cent choline. Positive controls (gm./100 gm.)	Plus 0·5 per cent carnitine (gm./100 gm.)	Plus 1·0 per cent carnitine (gm./100 gm.)
Total animals used	20	20	20	10 (2 per group)
1	54·2	10·9	58·6	58·5
2	55·4	12·4	55·0	57·2
3	52·2	19·9	55·4	47·5
4	59·0	11·2	51·3	47·1
5	60·7	22·5	53·0	62·1

The lipids from 300 ml. of foxhound serum were extracted with ethanol/ether and hydrolysed by boiling with methanolic hydrochloric acid (following the procedure of Binon and Deltour). The two fractions obtained by differential reineckate precipitation at *p*H 10 (voluminous) and *p*H 2 (trace) were examined by paper chromatography. They were run in the presence of silver nitrate[10] in ethanol/ammonium hydroxide/water (95 : 5 : 5) and in a second experiment in *iso*propanol/ammonium hydroxide/water (20 : 1 : 2). The spots were located with iodine and with potassium bismuth iodide. Choline was the only quaternary ammonium compound detected in both reineckate fractions. Direct chromatography of the phospholipid hydrolysate, without reineckate treatment, also failed to reveal the presence of carnitine.

In addition to the serum investigation the phospholipid fraction of beef muscle was examined. The fraction was obtained by petroleum ether/ethanol extraction followed by acetone precipitation[11]. The hydrolysed material showed no reineckate precipitate under acid conditions, and chromatography revealed choline as the only quaternary ammonium compound.

It thus appears that carnitine is not present in phospholipids of blood or muscle, and that it does not play a part in transmethylation reactions that lead to the formation of choline or betaine.

A detailed account of this work and further investigations into the role of carnitine will be published elsewhere.

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17-Oxosteroids of Pregnant Ewes' Urine

In view of the increasing use of steroid hormones and stilbene derivatives in agriculture and agricultural research, it was felt that it was necessary to investigate steroid excretion by the ewe.

The isolation of 5β-pregnane-3α:20α-diol from the urine of the pregnant ewe was recently reported by Robertson and Coulson[1]. As a continuation of this work the neutral ketonic fraction of pregnant ewes' urine was investigated.

22·5 l. of urine representing twenty 24-hr. collections from two ewes in the fourth month of pregnancy were acid hydrolysed and extracted in the usual way. The neutral extract was separated into ketonic and non-ketonic fractions by the method of Dorfman[2].

The ketonic fraction of 100 mgm. was then chromatographed on an alumina column but no crystalline fractions were obtained.

The residues from the column were bulked into four main fractions (*A*–*D*), and 1/100 aliquots from each of these fractions were then chromatographed on paper in each of the following systems: (1) 100–120 petroleum ether–propylene glycol, (2) Bush's system *A*, (3) toluene–propylene glycol.

A series of known steroids were also run to provide standards and the chromatograms were sprayed with a modified Zimmerman reagent to locate 17-oxosteroid-like material. These results are summarized in Table 1.

Table 1. Chromatography of the Neutral Ketonic Fraction of Pregnant Ewes' Urine

Fraction	Substance†	Approximate quantity present‡	R_F value* in system		
			Petroleum ether–propylene glycol	Bush *A*	Toluene–propylene glycol
		(μgm.)			
A	*A*(1)	5	0·2	0·23	0·6
	A(2)	10–20	0·58	0·83	1·0
B	*B*(1)	10	0·2	0·23	not resolved
	B(2)	10	0·58	0·83	1·0
	B(3)	5	not resolved	0·68	not resolved
C	*C*(1)	5	not resolved	not resolved	0·15
D	No 17-oxosteroids	—	—	—	—
	Androsterone		1·0	1·0	1·0
	Aetiocholanolone		0·6	0·85	1·0
	Dehydro*epi*androsterone		0·5	0·69	1·0
	$\Delta^{1,4}$ Androstadiene-3 : 17-dione		0·55	0·55	1·3
	Δ^{4} Androstene-3 : 17-dione		1·25	0·86	1·3

* The rates of flow are expressed relative to androsterone.

† Only those materials which gave purple colour reactions similar to 17-oxosteroids are recorded.

‡ The approximate quantity of material present was deduced by comparison of the spot produced with one produced by 20 μgm. of steroid, taking into account the fact that the lower limit of sensitivity of the reagent was about 2·5 μgm. of steroid per spot.

Material *A*(1) and *B*(1) were apparently the same substance but could not be identified from the standards. This material like *C*(1) was of low R_F value and was therefore of a more polar nature than the standards.

From a comparison of R_F values substances *A*(2) and *B*(2) were apparently identical with ætiocholanolone.

Substance *B*(3) which was only resolved from *B*(2) in the Bush system and was therefore of very similar R_F value to *B*(2) in the other systems was tentatively identified as dehydro*epi*androsterone.

As 1/100 aliquots were run on paper the total 17-oxosteroid content of the urine was probably of the order of 5 mgm., which correspond to an excretion-rate of 0·25 mgm. per sheep per 24 hr. This appears to be made up of 2 mgm. (100 μgm. per sheep per 24 hr.) of aetiocholanolone, 500 μgm. (25 μgm. per sheep per 24 hr.) of dehydro*epi*androsterone and 2·5 mgm. (125 μgm. per sheep per 24 hr.) of at least two other unidentified steroids.

Thus the 17-oxosteroid excretion in pregnant ewes' urine, like the pregnanediol excretion, is very small by comparison with human urinary excretion.

As a result of the small quantity of 17-oxosteroids present and the large quantities of other material encountered it was concluded that the accurate quantitative estimation of 17-oxosteroids in sheep's urine could not be carried out by the usual methods.

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Isolation of 17-*Epi*œstriol from the Urine of Pregnant Women

The isolation of 16α-hydroxyœstrone in 1957 by Marrian, Watson and Panattoni[1] led these authors to suggest that this compound might be the metabolic intermediate in the 'hydration' of œstrone to œstriol. In the same year, Brown and Marrian[2] reported that about 40 per cent of 16α-hydroxyœstrone when administered to human subjects was afterwards excreted in the urine as œstriol. Breuer, Nocke and Knuppen[3] found after incubation of 16α-hydroxyœstrone with slices of normal human liver in addition to œstriol a second metabolite which was identified as 17-*epi*œstriol (œstra-1,3,5-triene-3,16α,17α-triol). In view of these findings it seemed reasonable to assume that 17-*epi*œstriol might be a normally occurring metabolite of the œstrogens, and therefore, an attempt has been made to isolate 17-*epi*œstriol from urine during pregnancy.

Late-pregnancy urine was hydrolysed with concentrated hydrochloric acid, extracted with ether and the extract washed with an aqueous solution of sodium bicarbonate and water. The 'polar' fraction containing œstriol and its epimers was recovered by water extraction and then further purified by saponification. In order to separate the *cis*-glycols (16-*epi*œstriol and possibly 17-*epi*œstriol) from the *trans*-glycols (œstriol and 16,17-*epi*œstriol) the material was treated with anhydrous acetone containing 1 per cent hydrochloric acid. The acetonides were extracted with chloroform and hydrolysed with 0·5 *N* phosphoric acid. The fraction thus obtained was chromatographed in small portions on a large number of sheets of paper using the system formamide/chloroform. The areas corresponding to the position of 17-*epi*œstriol were eluted with methanol, the eluates combined and rechromatographed in the same system for 6 hr. After spraying the paper with Folin and Ciocalteu's reagent a blue spot was detected which had the same mobility (1·8 cm./hr.) as authentic 17-*epi*œstriol. In a second experiment, the areas expected to contain 17-*epi*œstriol were eluted, the eluates evaporated and subjected to sublimation under normal pressure. Crystals were obtained which showed the same melting point (233–235°) as authentic 17-*epi*œstriol. The material had the same absorption curve as 17-*epi*œstriol in the ultra-violet region (maximum at 279 mμ), with the Kober-reaction (maximum at 515 mμ) and with the sulphuric acid/water reaction (maxima at 286 and 456 mμ). The mobility of the fast black salt potassium derivative (0·33 cm./hr.) was identical with that of 17-*epi*œstriol when chromatographed in the system toluene/light petroleum/ethanol/water (200 : 100 : 30 : 70).

In view of the evidence presented here it is concluded that in addition to œstriol[4], 16-*epi*œstriol[5] and 16,17-*epi*œstriol[6], the fourth possible isomer, 17-*epi*œstriol, is present in human pregnancy urine.

As compared with œstriol, however, its concentration is very small. In a pooled late-pregnancy urine, the yield of 17-*epi*œstriol as determined by the Kober reaction was approx. 10 μgm./l., whereas the concentration of œstriol amounted to 15 mgm./l.

Full experimental details will be published elsewhere. I am grateful to Dr. R. Knuppen for preparing 17-*epi*œstriol, to Dr. W. Nocke for advice on the technique of the preparation and hydrolysis of 17-*epi*œstriol–acetonide and to Mrs. Brigitta Dumont and Miss Gerta Pangels for skilled technical assistance.

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Labelling of Deoxyribose with Carbon-14 in Relation to Incorporation of Phosphorus-32 into the Nucleotides of Deoxyribonucleic Acid of Rat Thymus Cells

It has previously been shown[1,2] that when rat thymus cells are incubated in the presence of glucose labelled with carbon-14, the isotope is incorporated to a different extent in the ribose moieties of the four individual types of nucleotide derived from ribonucleic acid. The ribose attached to the pyrimidine bases has a specific activity lower than that of the purine-bound ribose. The present report deals with experiments on the sugar component of deoxyribonucleic acid, and also with a comparison of carbon-14-labelling of deoxyribose and incorporation of phosphorus-32 into the nucleotides of deoxyribonucleic acid.

Male albino rats weighing about 150 gm. were used. The thymus glands were removed under ether anæsthesia; a suspension of the thymus cells was prepared[3] and the cells were incubated in the presence of glucose-^{14}C (generally labelled). At the end of the incubation the acid-soluble material and lipids were extracted from the thymus cells. The residue was extracted with 10 per cent sodium chloride solution at 100° C. to isolate the sodium nucleates, which were then fractionated into ribonucleotides and deoxyribonucleic acid by alkaline hydrolysis and subsequent acidification[4]. The deoxyribonucleic acid was degraded by deoxyribonuclease and snake venom to nucleosides which were separated by paper chromatography in *n*-butanol/ammonia[5]. Each of the nucleoside fractions was degraded[6] to give free deoxyribose, which was further purified by paper chromatography using ethyl acetate/acetic acid/water as solvent[7]. Deoxyribose was determined in an aliquot of the eluate by the diphenylamine reaction[8], and another aliquot was taken for radioactive assay.

Table 1 shows the specific activity of deoxyribose derived from the four nucleosides obtained from deoxyribonucleic acid. It can be seen that the incorporation of carbon-14 into the purine-bound deoxyribose is more than twenty times greater than the incorporation into the pyrimidine deoxyribose. This finding shows a similar trend to the results obtained with ribonucleic acid[2], although the difference between the values of specific activity of the purine ribose and the pyrimidine ribose was not as great as that found here for deoxyribose.

Table 1. Incorporation *in vitro* of Carbon-14 from Labelled Glucose into the Deoxyribose of Deoxyribonucleic Acid of Rat Thymus Cells

Source of deoxyribose	Specific activity of deoxyribose (counts/min./μmole)	Relative incorporation of carbon-14 into deoxyribose
Adenine deoxyriboside	325	100
Guanine deoxyriboside	420	129
Cytosine deoxyriboside	10	3
Thymidine	21	6

Each of two incubation vessels contained 6 ml. of cell suspension, obtained from eight thymus glands, in Krebs–Ringer phosphate solution (ref. 9) gassed with oxygen and containing glucose-^{14}C (generally labelled). Glucose concentration: 5 mgm./ml.; specific activity of glucose: $9{\cdot}89 \times 10^4$ counts/min./μmole. The vessels were shaken at 37·5° C. for 3 hr., the evolved carbon dioxide being absorbed in potassium hydroxide. At the end of incubation the contents of the two vessels were pooled.

In order to test whether the turnover of the phosphorus moiety of each of the deoxyribonucleotides follows a pattern similar to that of the corresponding deoxyribose moiety, experiments were carried out to determine the incorporation of phosphorus-32 into the four different types of nucleotide derived from deoxyribonucleic acid. Rat thymus cells were incubated in the presence of orthophosphate labelled with phosphorus-32. Deoxyribonucleic acid was isolated as described above and was degraded[10] by deoxyribonuclease and phosphodiesterase from rattle-snake venom[11]. The deoxyribonucleotides were separated using the paper electrophoresis technique of Markham and Smith[12], and their specific activities were then determined. The results of a typical experiment are shown in Table 2. It is clear that there is no difference between the incorporation of phosphorus-32 into the purine and the pyrimidine nucleotides, the specific activities of the four deoxyribonucleotides being of the same order. This finding is in sharp contrast to the observations made on the distribution of carbon-14 in the different deoxyribose moieties (Table 1), and also to the results reported for the sugar of ribonucleic acid where great differences were found between the specific activities of the ribose moieties of the different nucleotides[2].

The striking feature of these observations is the difference in pattern of incorporation of carbon-14 into the deoxyribose moieties of deoxyribonucleic acid and the incorporation of phosphorus-32 into the corresponding nucleotides. The difference in the degree of labelling of these two different moieties of a given nucleotide is of special interest in the study of the metabolism of deoxyribonucleic acid with the

Table 2. Incorporation *in vitro* of Phosphorus-32 into the Nucleotides derived from Deoxyribonucleic Acid of Rat Thymus Cells

Nucleotide isolated	Specific activity (counts/min./μmole)	Relative phosphorus-32 incorporation
Deoxyadenylic acid	465	100
Deoxyguanylic acid	576	124
Deoxycytidylic acid	502	108
Thymidylic acid	647	139

The incubation vessel contained 11 ml. of cell suspension, obtained from six thymus glands, in Krebs–Ringer bicarbonate gassed with 95 per cent oxygen – 5 per cent carbon dioxide (ref. 9). Orthophosphate labelled with phosphorus-32 was added to give a final concentration of 1 μc./ml. Glucose concentration was 5 mgm./ml. The vessel was shaken at 37·5° C. for 3 hr.

aid of labelled precursors. It indicates corresponding differences in the rates of turnover of the two moieties, the renewal of which presumably occurs while the nucleotides form part of the pool of free nucleotides of the cell constituting the precursors of deoxyribonucleic acid. It should be emphasized that the relative rates of turnover of these nucleotides, at least *in vitro*, evidently depend upon the moiety being studied.

It is not yet known whether similar differences in the pattern of incorporation of the two isotopes exist also between the nucleotides of ribonucleic acid; work is being carried out on this particular problem.

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ANIMAL PHYSIOLOGY

Failure of Growth in Disturbed Laboratory Rats

Laboratory rats can be very sensitive to disturbances of their accustomed environment or routine, and they may react by modifying their eating and drinking behaviour in various ways[1–4]. If some kinds of disturbance are prolonged, the body-weight may be affected, and we have previously found this a particularly useful measure: rats which were exposed to disturbances either lost weight or they failed to gain it as quickly as undisturbed controls[5,6].

In one of these investigations[5] adult rats were subjected to disturbances of a kind which often occurs incidentally during laboratory experiments: transfer to an unfamiliar room and cages, separation from cage mates, a new form of diet, oral injections. These changes were introduced concurrently, and by the end of the next 24 hr. the rats had eaten and drunk only about half their normal intake and had lost nearly 3 per cent of their body-weight. The environmental changes were maintained for three weeks; by then the rats had not yet made good the loss of weight: a control group had meanwhile gained more than 3 per cent.

Relatively commonplace events seemed, therefore, to have evoked a big reaction, and in the present investigation this kind of situation was analysed further and over a longer period of time. In particular, the aim was to study effects on body-weight: (*a*) when environmental changes were introduced gradually, that is, one by one, and time was allowed for the rats to become adapted before the next change was made; (*b*) during a subsequent period when no further changes were made and the rats were left to 'recover' undisturbed.

Male Lister hooded rats lived under uniform conditions, three to a cage, since weaning and were little handled. When they were 200–210 days old they were allocated at random to two groups of five rats. The 'undisturbed' control group remained in their home cages in the colony room throughout and were merely weighed daily. The 'disturbed' experimental group were also weighed daily, and in addition they were treated as follows:

(1) *Transfer to another room.* The rats stayed in their home cages but were transferred by trolley to another room nearby where the cages were again suspended in standard racks. The temperature (set by thermostat at 68° F.) and the general level of light and noise in the new room were roughly the same as in the colony room; humidity could not be controlled but the fluctuations when measured were fairly similar in the two rooms. The usual diet (41.*b*, pellets) and water continued to be available *ad lib.*

(2) *Change of diet.* Eight days later, a powdered form of diet 41.*b* was substituted for the pellets.

(3) *Segregation.* After a further 8 days, the rats were separated from their cage mates and were re-housed singly in unfamiliar cages of identical pattern.

(4) *Injections.* After 8 days of living singly, and daily thereafter, each rat was given orally by syringe 1 ml./kgm. tapwater.

(5) *Daily change of cage.* Eight days after the injections had begun, each rat was re-housed in an unfamiliar though otherwise similar cage each day. Thus, once an environmental change had been introduced it was maintained, so that by now the rats were living in the new room, on powder food, singly, with a daily injection and in a different cage each day.

(6) '*Recovery.*' After 12 days, no further changes were introduced, injections ceased, and the rats remained—still singly and with powder food—in the same cage for a final 16 days. Throughout the investigation the body-weights and food and water intake were determined, and any environmental changes were made daily between 2.30 and 3.30 p.m. The mean starting weights were: experimental group 317·4 gm., *S.D.* 33·6, controls 323·2 gm., *S.D.* 45·8, and the difference was not significant ($P > 0.05$). All rats seemed in normal physical health throughout.

Fig. 1 shows the mean gains or losses in body-weight for the two groups during the 60 days. The 'undisturbed' controls gained weight fairly steadily throughout, and by the end the average gain was 29·0 gm., *S.D.* 5·4, or about 9 per cent. In the experimental group, however, weights changed relatively little during the first 44 days while the environmental disturbances were taking place. Immediately after all but one of the disturbances there was if anything a slight drop in weight, of the order of 2–3 gm., but this had usually been made good by the time the next kind of disturbance was due; the greatest drop followed the introduction of the new diet, but even this was not statistically significant. The pattern of daily food and water intake roughly reflected the fluctuations in weight; the greatest drop occurred, again, just after the change of diet when the average

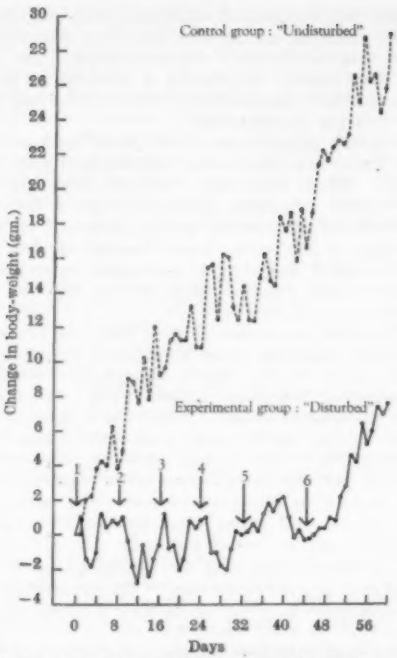

Fig. 1. Arrest of gain in weight in rats subjected to environmental changes. The control group remained undisturbed in the colony room throughout. The experimental group had successively the following treatments: (1) transfer to another room; (2) change in the form of diet; (3) segregation from cage mates; (4) daily oral injections; (5) daily change of cage; (6) 'recovery', that is, no further alterations in the environment were made. The arrows indicate when each kind of treatment began. Weight changes are expressed as mean gains or losses from the mean body-weight of each group at the beginning of the experiment

food and water intake was about a quarter less than usual. Thus at the end of the 'disturbed' period the experimental group still weighed almost exactly the same as at the beginning (mean change − 0·4 gm., *S.D.* 4·2); the controls had meanwhile gained 16·6 gm., *S.D.* 2·4. The net difference between the two groups was therefore 17·0 gm., and these changes in mean weight differ significantly between the two groups ($t = 7{\cdot}05$, $P < 0{\cdot}001$). When 'recovery' began, the weight of the experimental group immediately began to climb, and the graph suggests that they gained weight at a rate roughly parallel to that of the controls. By the end of the 16 days recovery they had gained 8·0 gm., *S.D.* 1·1, slightly less than the corresponding 12·4 gm., *S.D.* 3·9, gained by the controls. The net difference between the two groups at the end of the experiment was therefore 21·4 gm. ($t = 6{\cdot}14$, $P < 0{\cdot}001$), and this makes it seem unlikely that the experimental group was catching up. Food and water intake during the recovery period were very slightly higher than before but did not increase as clearly as body-weight.

These results suggest that the environmental changes led to a temporary arrest in the rats' normal weight gain. Since for practical reasons the order in which the changes were made was the same for all the rats, it is not strictly valid to compare the effects of the different kinds of change with each other. Superficially the effects of each kind of change were fairly similar, and the effect of the change of diet was possibly the greatest. Merely to move the rats from the colony room to another room at the beginning of the experiment (Fig. 1 (1)) had some effect, though this was smaller than the effect previously referred to of making various other changes concurrently[6].

A probable reason for the arrested gain in weight was that the disturbed rats temporarily ate and drank less than usual. Environmental changes of the kind described might, however, also have had other effects, like increased general activity[7,8], less-efficient assimilation of food[9], or loss of heat because of single living[10], and any of these could have helped to keep down body-weight. The experimental group was also, inevitably, handled slightly more than the controls, but handling probably benefits body-weight[11]. Whatever the exact explanation, the results illustrate that common laboratory procedures to which normally little importance might be attached can—at least where rats' body-weight is concerned—have sizeable and lasting adverse effects.

Effects of this kind can sometimes be mitigated by administering small doses of the tranquillizing drug chlorpromazine[6].

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Modification of Cholesterosis and Lipidosis of Rats maintained on an Atherogenic Diet

Although the liver is regarded as the primary organ of lipid metabolism, little is known of this metabolic process at the cellular level. Recognizing that the cellular composition of liver is approximately 61 per cent parenchymal and 33 per cent littoral cells[1], I attempted to clarify the participation of hepatic cells in lipid metabolism by studies on the lipid composition of isolated parenchymal and Kupffer cells[2]. This work showed, in reference to the isolated parenchymal cell, an elevated cholesterol-level in Kupffer cells which suggested that these cells actively participated in cholesterol metabolism. Subsequent work indicated that Kupffer cells probably are not involved in the uptake of plasma cholesterol but do participate in its biotransformation or excretion[3].

The present work was designed to investigate the relationship between reticuloendothelial activity, and the ability of the animal to handle an exogenous cholesterol load. If Kupffer cells are involved in the biotransformation or excretion of cholesterol, then during reticuloendothelial hyperactivity one would anticipate increased tolerance to ingested cholesterol.

Table 1. Influence of Zymosan on Hepatic Lipids* of Normal and Cholesterol-Fed Rats

Group	No.	Body-weight (gm.)		Liver (per cent body-weight)	Spleen (per cent body-weight)	Cholesterol			Neutral fat
		Initial	Final			Free	Ester	Total	
Control	9	209 ± 6·6	265 ± 11·8	3·7 ± 0·19	0·23 ± 0·01	1·82 ± 0·08	0·71 ± 0·11	2·53 ± 0·10	9·14 ± 2·25
Control and zymosan	9	206 ± 11·5	211 ± 6·1	6·3 ± 0·24	1·10 ± 0·18	2·18 ± 0·09	0·35 ± 0·12	2·54 ± 0·14	6·81 ± 0·71
Cholesterol-fed	9	201 ± 6·6	198 ± 13·2	5·4 ± 0·25	0·24 ± 0·01	4·60 ± 0·29	50·56 ± 4·25	54·57 ± 4·55	33·93 ± 3·34
Cholesterol-fed and zymosan	9	212 ± 6·8	168 ± 4·9	7·1 ± 0·48	0·75 ± 0·09	3·45 ± 0·15	17·20 ± 2·74	20·98 ± 2·77	17·89 ± 1·82

* Lipid values are expressed as mgm./gm. of fresh tissue weight ± standard error.

This would be reflected by lower tissue cholesterol-levels. Since reticuloendothelial blockage cannot be produced[4], the influence of reticuloendothelial hyperactivity on liver cholesterol-levels was studied in rats maintained on normal and high cholesterol, high fat diets. The reticuloendothelium was stimulated by the intravenous injection of the yeast extract, zymosan, in the amount of 10 mgm. administered on alternate days. Thirty-six male rats were initially employed, 9 normal rats served as controls and received saline injections, while 9 additional normal rats received zymosan. The remaining 18 rats, 9 of which received zymosan, were fed an atherogenic diet similar to that employed by O'Neal *et al.*[5], which contained the following:

	Per cent		Per cent
Casein 'vitamin free'	19·9	Thiouracil	0·3
Sucrose	18·1	Choline chloride	0·2
Salt mix (U.S.P. XIV)	7·3	Sodium cholate	1·8
Alphacel (non-nutritive bulk)	9·1	Butter	37·0
Vitamin diet fortification mixture	1·8	Cholesterol	4·5

Daily determinations were made on body-weight and food-intake. At the end of the 14-day period liver total and free cholesterol, phospholipid and neutral fat were determined as previously described[6].

In agreement with previous observations[7] the administration of zymosan to rats maintained on 'Purina' show significantly increased weight of liver and spleen. The liver free and ester cholesterol fractions were not significantly altered in the normal rats given zymosan. Maintenance of rats on the atherogenic diet for 14 days significantly elevated the free cholesterol and profoundly increased the ester cholesterol and neutral fat. The administration of zymosan to rats maintained on the diet induced a comparable increase in liver and spleen weight despite the elevated dietary thiouracil level. Zymosan significantly reduced the accumulation of free and ester cholesterol and neutral fat in the liver. No correlation could be demonstrated between changes in body-weight and liver cholesterol-levels. Dietary-intake was not significantly different in the saline- and zymosan-treated groups maintained on the atherogenic diet. A significant reduction in plasma ester cholesterol was also noted in the zymosan-treated group, although no change was observed in the concentration of various lipid fractions of the spleen.

A pair-feeding experiment was also carried out for a 5-day period with 6 male rats maintained on 'Purina' chow to which 1 per cent cholesterol and 0·5 per cent sodium cholate was added. This would eliminate any question of body-weight alterations and also evaluate the effectiveness of zymosan in preventing liver cholesterol accumulation at lower levels of dietary cholesterol intake. These animals lost a mean 9 per cent of their initial weight. In the untreated cholesterol-fed group the liver ester cholesterol concentration was significantly elevated (Table 2). As observed in the previous studies, a significant reduction (88 per cent) occurred in the ester cholesterol fraction of the rats which were daily injected intravenously with zymosan in the amount of 5 mgm./day.

It is apparent that a major determinant to elevated plasma and liver cholesterol-levels of rats maintained on a high cholesterol diet is the functional state of the reticuloendothelium and specifically the number and activity of Kupffer cells.

Table 2. Effect of Zymosan on Liver Cholesterol-Levels* of Pair-Fed Rats on a 1 per cent Cholesterol Diet

Group	Body-weight (per cent)		Cholesterol		
	Liver	Spleen	Total	Free	Ester
Normal	3·41	0·19	2·16	1·91	0·25
Cholesterol-fed	3·01	0·24	18·03	3·20	14·83
Cholesterol-fed + zymosan	3·95	0·69	4·48	2·26	1·82

* Mean values are expressed as mgm. of cholesterol per gm. of fresh tissue.

Stambul[8] has previously summarized evidence for the role of Kupffer cells in the biliary excretion of cholesterol. In view of our previous observations[2,3] and the known mode of excretion of cholesterol which in the rat is an array of bile acids, the following concept can be proposed. This concept indicates the possible mechanism whereby zymosan prevents the accumulation of liver and plasma cholesterol and the possible etiology of hypercholesterolæmia and lipidosis in the untreated animals:

Elevated dietary cholesterol
↓
Elevated liver cholesterol
↓
Kupffer cell excretion of cholesterol
↓

Normal untreated rat (excretory limit of Kupffer cells is surpassed)	*Zymosan-treated rat* (Kupffer cell hyperplasia and hyperfunction)
↓	↓
'Reduced' biliary cholesterol and bile acid-levels (relative to intake)	'Enhanced' biliary cholesterol and bile acid-levels
↓	↓
'Reduced' biliary excretion	'Enhanced' biliary excretion
↓	↓
leading to	leading to
↓	↓
Elevated liver cholesterol (possibly resulting in impaired Kupffer cell activity)	Reduced liver cholesterol
↓	↓
Elevation in plasma cholesterol	Reduced plasma cholesterol
↓	↓
Atherogenesis	Possible decrease in atherogenesis

In view of the functional complexity of the reticuloendothelium, and the role of zymosan in immunological mechanisms, other phases of reticuloendothelial activity besides reticuloendothelial involvement in cholesterol metabolism could be the mechanism of the protective action of zymosan. However, the present findings apparently demonstrate a new concept in the regulation and prevention of hepatic lipidosis and cholesterosis and possibly experimental atherosclerosis through the activation of the reticuloendothelium.

Work to substantiate further this hypothesis is now in progress.

The accumulation of lipid in Kupffer cells is reported to be most marked in diabetes[8], a condition associated with impaired reticuloendothelial activity[10] as well as hyperlipæmia and increased incidence of atherosclerosis.

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Diathelic Immunization of Sheep against a Rat Cancer

The term 'diathelic immunization' has been introduced by B. Campbell *et al.*[1], who instilled different antigens into the orifice of the milk gland (in cows) and obtained colostrum and milk with high titres of antibodies against the antigens used. They consider the milk gland as an exocrine reticuloendothelial gland.

It has been shown by previous work that resistant rats (strain *bWr*, or black-Walker-resistant, inbred in our laboratory) produce, after implantation of the Walker 256 tumour, factors inhibiting the growth of this tumour in susceptible rats, when resistant immune blood serum is injected into them intraperitoneally[2], and that susceptible rat sucklings are protected against the growth of the tumour by the ingested milk when nursed by the resistant immune rat females[3].

Further, it has been shown that spleens of resistant rats immunized by the tumour *in vivo* continue the production of antitumour factors when explanted in tissue culture[4], and that an active immunization *in vitro* of spleens from normal resistant rats against the tumour used is possible[5].

In the present experiments, we instilled repeatedly, at weekly intervals, by means of a glass canule, several million of live Walker 256 tumour cells suspended in about 0·5 ml. of saline into the orifice of the milk glands of two sheep a month or more after parturition. Instillation was carried out on the evening after the last (third) day's milking. 12 hr. later (on the next morning) the milking was continued.

There was a massive cellular reaction in the milk from the instilled udders, changing gradually, in the course of the immunization, from nearly exclusively polymorphonuclear (segmented) leucocytes to more and more mononuclear cells with a large plasmatic component. (This cellular reaction will be described in detail and analysed in a separate communication.) There was also a strong decline in the milk output beginning at 18 hr. after instillation, but in the following 3–5 days milk output returned nearly to normal. There were no signs of bacterial inflammation of the instilled udders or of the animals themselves, although some capsulated bacteria have been seen in cell-preparations from the milk; milking was done under the usual non-aseptic conditions. The cellular reaction as well as the inhibition of lactation seem to vary from individual to individual; both were much stronger in one sheep than in the second.

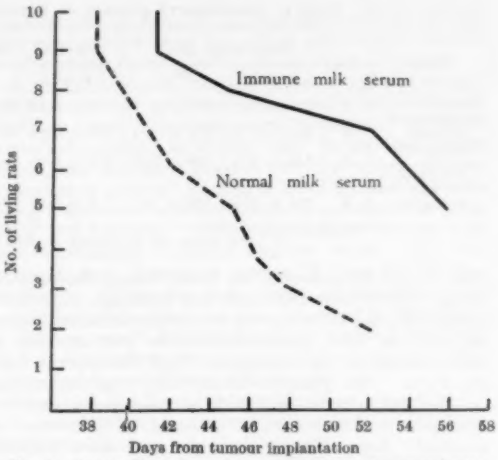

Fig. 1. Deaths from tumour in rats injected with normal and immune milk serum

The 'immune' milk was used in several ways.

(1) A neutralization test was performed. Rats were implanted with equal doses of the Walker 256 tumour cells, which had been incubated for 3 hr. at 37° C. in the normal and immune milk (only the milk fat was separated by centrifugation). After incubation, the cells were centrifuged from the milk and resuspended in saline before implantation. A control set of rats was implanted with non-incubated tumour cells (from the same original suspension), in saline. Results are given in Table 1.

Table 1

Incubation	Tumours*	
None	7/10	(70 per cent)
In normal milk	17/20	(85 per cent)
In immune milk	9/20	(45 per cent)

* Ratios of rats with tumours to the total number of animals used; after 30 days no new tumours appeared.

(2) Milk serum was prepared by adding some drops of dairy rennet and centrifuging the curdled milk, and injected after Seitz-filtration intraperitoneally into susceptible rats bearing implants of equal numbers of live Walker 256 cells. Results of two groups of 10 male rats weighing 120–150 gm. at the start of the experiment, and given, from the day of tumour implantation, 2 ml. daily of normal or immune milk serum for 40 days, are illustrated in Fig. 1. In the normal series there are 2 non-takes in 10, in the immune series 5 non-takes in 10.

It is to be noted that the gains in weight of rats given the immune milk serum were lower than of those given the normal milk serum or of the controls. The gains in weight of different groups after 15 days from the beginning of the experiment are given in Table 2.

Table 2

Injections	Mean gain in weight
None	16 per cent
Normal milk serum	15 per cent
Immune milk serum	8 per cent

After 15 days, the weight control is obscured by the growing tumours. On the whole, the anti-rat component of the heterologous (sheep) immune milk under given conditions seems negligible; all rats surviving without tumours, both in the experimental as well as in the control groups, seem undamaged and live normally to date.

(3) Cytotoxic effect of the immune milk serum was proved by the method of unstained cell count[6]. Freshly prepared tumour cells were suspended in normal and immune milk serum, counted, incubated at 37° C. for 4 hr. and counted again. Table 3 indicates results of these counts on 6 subsequent days, where the influence of milk sera from three different sheep after different numbers of immunizations are compared. In all these experiments, drops of complement were added (guinea pig serum); but we have found that fresh immune milk serum has a cytotoxic activity of equal degree without the addition of complement.

Table 3

Sheep No.	No. of immunizations	Cell count (per cent) before incubation	Cell count (per cent) after incubation, mean from 6 days	Range
1	none	100	96	82–100
2	3	100	57	48–67
3	5	100	18	10–26

These results, considered with previous work, seem to prove that any system capable of immune reaction is able to produce anti-tumour factors passively transmissible, and active in inhibiting tumour growth in susceptible animals. Furthermore, there seems to be a possibility of producing relatively large amounts of these active substances by a procedure which is very simple and obviously harmless for the producing animal. Thus some kind of immunotherapy could be used in combination with other therapeutic means in cancer.

Attempts to separate the active substances from the milk serum (as milk globulins), as well as to purify them from the anti-species component, are proceeding. Also the possible role of the cellular milk reaction and the eventual use of such cells are being considered.

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Fibrinolytic Activity of Cirrhotic Liver

Several investigators have observed increased fibrinolytic activity in the circulating blood in cases of liver cirrhosis in man[1–4]. The cause of this activity is unknown, though a toxic effect similar to that produced in dogs by chloroform or peptone has been suggested. Such a mechanism could possibly be involved in an acute process, but could barely explain the prolonged periods of increased fibrinolytic activity observed in cases of liver cirrhosis.

A mechanism by which the fibrinolytic system in blood is activated by an activator of plasminogen released from injured tissue is apparently excluded, since such fibrinolytic activity has been reported to be absent from liver tissue[5–8].

We have now investigated the fibrinolytic activity of tissue from a series of cirrhotic livers, estimating the concentrations of plasminogen activator by a quantitative method[9]. The results are given in Table 1. It is seen that the samples from the cirrhotic livers show varying degrees of fibrinolytic activity. When compared with the concentrations in normal human organs[8] some of the pathological liver samples even range among the most active tissues in the human organism. Another significant observation is a slight increase in activity of apparently normal livers with age (Table 1).

Table 1. Fibrinolytic Activity of Apparently Normal and Cirrhotic Human Livers estimated as Concentration of Plasminogen Activator in Units of a Standard Preparation per gm. Fresh Tissue

Normal group			Cirrhotic group		
Age	Sex	Activity	Age	Sex	Activity
42	M	0	40	M	1,935
55	M	0	67	F	80
59	F	0	68	M	650
60	M	27	68	M	262
62	F	0	70	F	18
64	M	11	74	M	63
65	M	0	76	F	456
66	M	19	77	M	935
66	M	1	78	M	1,781
69	F	1	78	F	205
72	M	0	80	M	188
73	F	41			
74	M	1			
74	M	42			
74	M	0			
78	F	28			
80	M	75			
80	F	48			
82	F	160			
83	M	0			

In accordance with views previously presented[10] fibrinolysis participates in wound healing. There are now several indications that vascularized connective tissue, occurring normally in the organism or formed as response to tissue injury, is characterized by high fibrinolytic activity caused by a plasminogen activator. Thus normal animal and human meninges are among the most active tissues so far investigated[11]. High activity was also recorded in the adventitia of arteries[12] or in the walls of veins[13] as well as in the kidney capsula[14]. The activity of the arterial adventitia increases with age[15], probably reflecting increased vascularization. Similarly, high fibrinolytic activity was found in connective tissue from samples of healed human myocardial infarcts[16] in contrast to the fairly low activity of normal human myocardium. The last two examples apparently represent a response to tissue injury similar to that occurring in liver cirrhosis or produced during ageing. The lack of fibrinolytic activity of blood in cases of primary carcinoma of the liver[8] probably points to a disturbed tissue repair process.

Since plasminogen is probably formed in the liver, it is easy to visualize that dangerous conditions

could arise when high concentrations of a plasminogen activator are found in close contact with plasminogen-producing liver cells. Apart from interfering with local wound healing and tissue repair, fibrinolytic activity could easily escape into the blood system. Hence, it is possible to understand the physiological basis of the morbidity of diseases leading to cirrhosis of the liver.

The results are also of interest in connexion with the low incidence of arterial disease recorded in patients with liver cirrhosis by some authors. The observations support the thrombogenic theory of the pathogenesis of arteriosclerosis, as set forth by Duguid[17,18], and strengthen the concept of a dynamic balance between fibrin formation and fibrinolysis as a regulator of this process[18,19].

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Rapid Contractile Properties of Isolated Mammalian Arteries

Strong indirect evidence is now accumulating[1,2] in support of the old idea that large mammalian arteries may be capable of contracting and relaxing at least as rapidly as the heart. Direct evidence based on studies of isolated arteries is still lacking, and this remains a major stumbling block in accepting the implications of much of the recent work.

Paton's technique[3] has been used to study the behaviour of 2–3 cm. lengths of dog's common carotid, femoral, hepatic and splenic arteries, and of sheep's hepatic and splenic arteries. The excised artery was tied on a glass cannula which formed a closed system connected to a manometer (Hansen condenser). The free end and any branches were ligated with fine silk, and the artery was stretched to about three-quarters of its natural length by a stiff silver wire passed through the cannula and along the lumen of the artery. This wire electrode was led through a seal into the air, and another silver electrode dipped into the bath in which the artery was immersed. Tyrode's solution at 37° C. was used in most experiments, and saturated with 5 per cent carbon dioxide and 95 per cent oxygen. From ½ to 4 hr. after excision all the 34 arteries examined were capable of raising the pressure within the closed system when an electrical stimulus was applied across the two electrodes. To square-wave stimuli the chronaxie was about 20 m.sec. and the rheobase 1–4 V. Responses were obtained equally easily whether the central lumen electrode was positive or negative. The highest rise of pressure obtained with a single shock (of an intensity and duration just less than that which caused irreversible damage to the preparation) was 15 mm. mercury. Much higher pressures could be obtained by repetitive stimulation. It was difficult to elicit any response if the starting pressure in the system exceeded 200 mm. mercury, and low pressures were used in most experiments because of the difficulty of stopping very small leaks.

The time course of a typical single contraction is shown in Fig. 1*A*, and the latency of onset of the contraction is shown at a faster film speed in Fig. 1*B*. Latency is 80 m.sec., time to peak pressure 2–3 sec., and time to full relaxation 5–10 sec. The speed of relaxation was usually greater at high internal pressures, at least within the physiological range. The contraction was reversibly abolished by increasing external potassium concentration to 130 m.equiv./l. (isosmotic with normal Tyrode solution); but it could still be elicited in the presence of atropine (10^{-7}) and dibenyline (10^{-6}) which had been allowed to act for 30 min. Slow repetitive stimulation produced pressure oscillations at frequencies up to about 0·7 c./s. (Fig. 2*A*). If an oscillating pressure was introduced into the system, the amplitude of oscillation was increased by stimulation (Fig. 2*B*), presumably because of increased rigidity of the muscular wall. The long chronaxie and the failure of drugs to influence contraction indicate that muscle cells are being excited directly. So far it has not proved possible to excite contraction through nerves, presumably because in this preparation the nerve supply is damaged. Even when arteries were tested in fresh plasma 5 min. after excision, there was no evidence at all of excitation of nerves. By analogy with other excitable tissues, it seems probable that

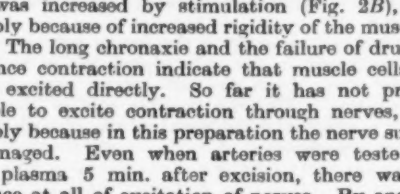

Fig. 1. Time-course of the contraction to a single stimulus (*S*) of a 2-cm. length of sheep's hepatic artery. (*A*) From above down: the stimulus (18 V., 20 m.sec., isolated from earth and fed to the cathode-ray oscillograph through capacitors); lumen pressure (scale on left in mm. mercury); time marking (½ sec.). (*B*) Onset of a contraction (at a faster film-speed) following a stimulus of 120 V. for 150 μsec.: time marking, ½ sec.

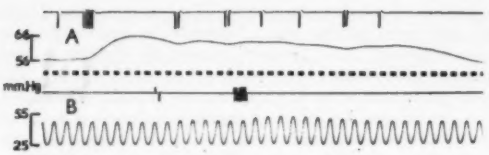

Fig. 2. (*A*) Response of a dog's hepatic artery to short bursts of repetitive stimulation. Top trace shows the stimulus record (retouched) and lower trace the pressure record. (*B*) Effect of an oscillating pressure introduced in the same preparation. Stimuli (upper trace, retouched) cause a rise of mean pressure and of oscillation amplitude (lower trace). Time marking ($\frac{1}{4}$ sec.) in between the records is the same for both

excitation through the normal nerve supply will produce more rapid effects.

Since efferent sympathetic activity normally occurs in bursts with a cardiac rhythm[4], it seems possible that rapid response of large arteries to such nervous activity could explain a number of curious phenomena observed in the peripheral arterial pulse contour, notably the augmentation of systolic peak pressure towards the periphery and perhaps also the dicrotic wave. It is noteworthy that atropine and procaine can abolish both these phenomena[5], even though there may be no change in mean arterial pressure.

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Thyroidal Control of Radiophosphorus Metabolism in Salmon

The part played by the thyroid gland in teleost metabolism has been investigated by many workers. In cold-blooded vertebrates it appears to be concerned more with growth than with general metabolism[1]. However, there is a great deal of controversy on practically every aspect of thyroid physiology. In higher vertebrates, the parathyroid plays an important part in the mineral metabolism. Fishes have, so far as known, no parathyroid. It has been suggested[2] that the ultimobranchial body in the teleost is the homologue of the parathyroid but as yet nothing positive has been established regarding this hypothesis. Fishes are able to control mineral metabolism within narrow limits; but there is scarcely any information concerning the role of the endocrines in this regulation. Radioisotopes are being used to carry out experiments to find out whether the thyroid gland has any influence on mineral metabolism in fishes.

In fishes the thyroid gland is divided into innumerable follicles in the region of the ventral aorta, hence surgical thyroidectomy is impossible. Yearling salmon, *Salmo salar* L., were divided into two groups of which one was maintained in 0·3 per cent solution of thiourea, referred below as treated. The other was used as control. The fishes were kept in thiourea solution for two weeks, the solution being changed every three days. After two weeks the fish were transferred to fresh aquaria to which sufficient phosphorus-32 had been added to give an activity of 2,500 counts per min. per ml. Aquaria for treated fish also contained 0·3 per cent solution of thiourea. At regular intervals starting from 2 hr. the tissues (liver, kidney, muscle and bone) were prepared for counting. The readings were corrected for decay and checked against a uranium standard. Carrier-free phosphorus-32 used was received from Atomic Energy of Canada, Ltd., in the form of phosphoric acid in diluted hydrochloric acid. In both the sets of experiments, bone took up the maximum activity, followed by liver, kidney and muscles. The uptake was always more in the treated set than the control. In the control, 40·1 per cent of phosphorus-32 was absorbed, whereas in the treated 50·3 per cent was utilized.

Another set of experiments was arranged to throw further light on the problem. The fishes were divided into three groups. One of them was injected with 0·2 ml. of 0·1 per cent solution of thiourea, the other with 0·2 ml. of 0·1 per cent solution of l-thyroxine and the third with 0·2 ml. physiological saline to serve as control. The injections were repeated again after three days. After a lapse of three days the fish were transferred to solutions of phosphorus-32 which gave an activity of 2,500 counts per min. per ml. In these experiments the uptake of radiophosphorus in bone and liver was studied. In the control, the fishes took up 39 per cent, fishes injected with thiourea absorbed 52 per cent and thyroxine-injected fishes utilized 63 per cent of phosphorus-32.

Thiourea had been used in the above experiments to destroy the thyroid gland and so to check its activity; but the histological studies showed that it was not achieved. Thyroid follicles were still present lined with low epithelial cells and were full of colloid. Administration of antithyroid drugs either abolishes or retards the ability of thyroid gland to synthesize thyroxine[3]. As a consequence of the cessation of thyroxine synthesis, the level of circulating hormone falls and the pituitary immediately responds by secreting additional amounts of thyrotropin which stimulates the thyroid so that hypertrophy of the gland results. This then shows that destruction of thyroid can only be achieved after treating the fishes with antithyroid drugs for considerably longer times.

The results of the experiments can be interpreted that in the fishes treated with thiourea the thyroid was stimulated indirectly (by thyrotropin secreted by the pituitary gland) and so the uptake of radiophosphorus was more than the control. In fishes treated with thyroxine the stimulation was direct and so the uptake was maximum. Detailed results of the experiments will be published elsewhere.

Complete thyroidectomy can be achieved by repeated doses of radioiodine[4]. Further work to study the effect of hypophysectomy and destruction of thyroid by radioiodine upon mineral metabolism is under investigation.

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Use of Chorionic Gonadotropin to prevent Early Embryonic Mortality in Temporarily Fasted Mice

When studying the pathogenesis of the infertility in female mice caused by depriving them of all food for short periods during early gestation[1], it was found that the immediate cause was either failure of implantation or death of the embryo after implantation. In the latter case, it appeared from the histopathology that the primary lesion occurred in the deciduoma. This was followed by the death of the embryo, possibly due to interference with its nutrition.

The minimal starvation required was the 48-hr. period from the fourth to sixth day after œstrus or third to fifth day after the formation of the copulation plug. Such fasting rendered all matings infertile. However, when injections of 5 I.U. of chorionic gonadotropin were given once daily to each of ten mice during the period when they were being starved, the embryos of all mice survived until at least the third day after the end of the fast. When examined at this time none of the twelve control mice, fasted but not injected, was pregnant. It was assumed from the results of earlier work that embryos had developed but had died and been reabsorbed. When chorionic gonadotropin was given to 16 mice in a third group, over the period from the start of starvation until five days after its end, the embryos of ten appeared normal on the sixth day after the end of fasting. The embryos of three were starting to degenerate and three mice were not pregnant. Progesterone in daily doses of 0·5 mgm. had a similar protective effect.

This suggests that the pathogenesis of the embryonic mortality involves the anterior pituitary–ovarian endocrine system.

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Oxygen Consumption by Tissues from Rats injected with L- or D-Thyroxine

It has been shown by a number of investigators that L-thyroxine is more active *in vivo* than is D-thyroxine[1]. In most *in vitro* systems, however, the D- and L-isomers are equally effective. The equal activity of D- and L-thyroxine in altering the morphology of mitochondria and in 'uncoupling' oxidative phosphorylation are examples of this[2,3]. Previous experiments[4] in this laboratory have compared the distribution and excretion of labelled D- and L-thyroxine labelled with iodine-131 following a single injection of a tracer quantity of each compound into the tail vein of the rat. Initially, D-thyroxine was concentrated to a greater extent in the liver and kidney than was L-thyroxine, but after 24 hr. the concentrations were approximately equal. However, the concentration of D-thyroxine in tissues such as muscle, brain and skin was much less than the concentration of L-thyroxine. This difference in distribution to the peripheral tissues was of such magnitude as to suggest a possible basis for the different activities of the two isomers *in vivo*. Others have shown[5,6] that the oxygen consumption of certain tissues (for example, liver, kidney and muscle) from animals injected with DL-thyroxine is significantly greater than normal, whereas that of other tissues (for example, brain) is not increased. The current investigation was undertaken to determine whether the differences demonstrated in the distribution of the two isomers could be correlated with a difference in their ability to stimulate the oxygen consumption of the several tissues.

Adult male Wistar rats, 4–6 weeks post-thyroidectomy, were used in this experiment. The treated animals were injected subcutaneously for 4 days with either D- or L-thyroxine (6 mgm./kgm.). (D-thyroxine was provided through the kindness of Dr. L. G. Ginger, of Travenol Laboratories, Inc., Morton Grove, Illinois. L-thyroxine was furnished through the kindness of Dr. A. E. Heming, of Smith, Kline and French Laboratories, Philadelphia, Pa.) The sodium salt of each isomer was dissolved in 0·02 *N* sodium hydroxide and 0·9 per cent sodium chloride. All animals were fasted 24 hr. before being anæsthetized with ether and exsanguinated. The various tissues were rapidly excised and placed in ice-cold Krebs–Ringer–phosphate solution. All tissues were prepared in duplicate. Liver, kidney and heart slices prepared by the Deutsch technique[7] were made smaller by cutting with scissors. Each diaphragm was cleared of fat and connective tissue, and its central portion was removed; the hemi-diaphragms then were placed in separate flasks. Specimens of brain were prepared by removing the larger tracts of white matter and forcing the remaining tissue through a syringe and No. 18 needle. After weighing, the tissues were placed in chilled Warburg flasks containing the incubation medium (Krebs–Ringer solution buffered with 0·01 *M* sodium phosphate with 100 mgm. per cent glucose). The flasks were gassed with 100 per cent oxygen for 5 min.; oxygen consumption was determined at 37° C.

It may be noted in Table 1 that with slices of liver from animals injected with either D- or L-thyroxine the oxygen consumption is almost identical; in both cases the Q_{O_2} is significantly greater than that of the control. The same result was also obtained with kidney slices. With heart and diaphragm, on the other hand, there is a significant difference between the animals injected with L-thyroxine and those injected with D-thyroxine; in both tissues the Q_{O_2}

Table 1. Oxygen Consumption by Various Tissues from Rats injected with L- or D-Thyroxine

	Control Q_{O_2} (10 rats)	L-Thyroxine Q_{O_2} (10 rats)	D-Thyroxine Q_{O_2} (10 rats)	*P* Control vs. L-thyroxine	*P* Control vs. D-thyroxine	*P* L-Thyroxine vs. D-thyroxine
Liver	1·40 ± 0·06*	1·94 ± 0·03	1·91 ± 0·07	< 0·001	< 0·001	> 0·1
Kidney	3·03 ± 0·13	3·79 ± 0·19	3·84 ± 0·11	< 0·01	< 0·001	> 0·01
Heart	1·21 ± 0·06	1·51 ± 0·08	1·30 ± 0·04	< 0·01	< 0·001	< 0·001
Diaphragm	1·11 ± 0·03	1·48 ± 0·04	1·29 ± 0·04	< 0·001	< 0·001	< 0·01
Brain	1·66 ± 0·04	1·51 ± 0·04	1·60 ± 0·04	= 0·01	> 0·1	> 0·1

* Standard error of the mean, Q_{O_2} = cu.mm. of oxygen per mgm. wet weight per hr.

was higher with tissues from animals injected with the L-isomer. The QO_2 of brain was slightly lower than control values in both series of treated animals. The present results support the thesis that the difference in physiological activity between the two isomers of thyroxine is probably secondary to their different distributions *in vivo*.

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Pitch Discrimination in Orthoptera (Insecta) demonstrated by Responses of Central Auditory Neurones

FOR about twenty years, since Pumphrey's review of hearing in insects[1], the commonly accepted view has been that the auditory organs of insects convey to the central nervous system considerable data about the pattern of amplitude of impinging sounds. There has been, on the other hand, no good evidence that the primary sensory nerves can or must convey cues as to the pitch of a sound stimulus and there has been no good evidence that the central nervous system responds differentially to one pitch rather than another, irrespective of intensity.

By recording from the pro-mesothoracic connectives of *Locusta migratoria* and *Schistocerca gregaria* (Acrididae) or from the cervical connectives of *Acheta domestica* (Gryllidae) with external electrodes, it is possible to identify a few ascending internuncial neurones which are excited at the sudden onset of a pure tone or short pulse of sound. The receptor is the tympanal organ, as may be shown by section of its nerve. The curve of threshold strength plotted against stimulus pitch for the single post-ganglionic neurone with the lowest threshold does not correspond with the analogous curve obtained by recording the summed action potentials of the sensory nerve, as initiated by the same stimuli. When recording from the sensory nerve the threshold was taken to be the stimulus strength required to produce a response of a fixed height on the oscilloscope screen, about one-twentieth of the maximal response.

The threshold strength of sound pulses required to elicit a response in a post-ganglionic neurone is raised by the simultaneous sounding of a continuous note. At the same time the pitch range of maximum sensitivity is moved as shown in Fig. 1. The direction of the shift of optimum pitch is away from the pitch of the continuous note. These results have been obtained with each of the above species of Orthoptera.

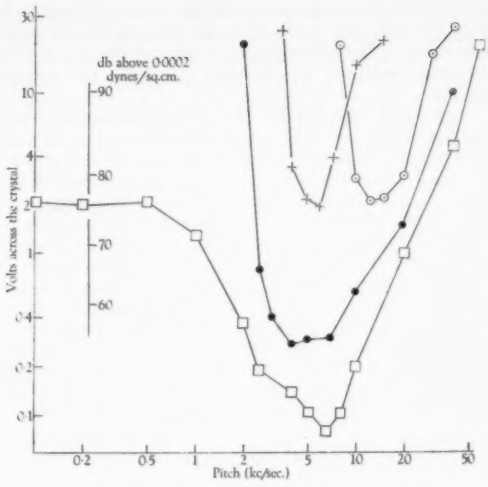

Fig. 1. Sound intensity threshold curves for auditory responses of *Locusta migratoria* with tone pulses of various pitch. □, From the tympanal nerve, the threshold being taken as the intensity required to give a twentieth of maximal response height. ●, From a single ascending neurone of the ventral cord. +, From the same neurone in the presence of a continuous tone at 15 kc./s. ⊙, From the same neurone with a continuous tone of 4 kc./s. Each point is the average of two readings, one taken ascending, the other descending the scale. The ordinate of sound intensity (db. above 0·0002 dynes/sq. cm.) is useful only up to 15 kc./s. and in the lower ranges is accurate to about 10 per cent

The difference between the pre- and post-ganglionic threshold curves is such that the metathoracic ganglion of the locusts responds differentially in favour of tone pulses of high pitch and rejects those of low pitch although they excite axons of the tympanic nerve. In the cricket, on the contrary, the prothoracic ganglion discriminates in favour of pulses in a low pitch-range of 0·5–3 kc./s., though the thresholds measured in the tympanic nerve do not begin to rise steeply until a range of 20–30 kc./s. is reached. Therefore, this evidence of discrimination indicates that the ganglion 'selects' certain axons, and this in turn means that discrimination has already occurred at the sense organ although formerly not observed by electrical recording from the whole bundle. The second piece of evidence, that the optimum pitch for the response to a pulse is shifted by a continuous note of differing pitch, does not indicate whether the mechanism lies in the ganglion or in the sense organ. A suggested explanation of these two sets of results is that there are at least two groups of sensory neurones, one group more easily excited by pulses of low pitch, one by pulses of high pitch. The group of neurones which become accommodated to a continuous note of one pitch would not then include those which are accommodated to a note of widely differing pitch.

Confirmation that different groups of sensory neurones are excited by the sudden onset of pure tone pulses of differing pitch comes from careful examination of the summed action potentials of whole tympanic nerves of the above two species of Acrididae. In preparations in which there is a favourable arrangement of the electrodes in relation to the short-circuiting of action currents, the summed action potentials initiated by pulses of one pitch cannot be matched in exact form by those initiated by pulses which differ only in pitch, no matter how relative stimulus intensities are adjusted. The response is of a

number of axons in each of which there appears to be only one impulse when sound pulses of 10–20 m.sec. are used. Therefore sound pulses of differing pitch initiate impulses in distinct groups of sensory axons.

A possible mechanism for pitch discrimination is suggested by the structure of the tympanal sense organ of the above species. The sensory neurones are not situated all at the same point but are separated into groups. In agreement with the arguments of Pumphrey[1] the sense organ behaves as a displacement receptor without resonance, but it is still possible for pulses of differing pitch to initiate differing modes of vibration so that the groups of sensory neurones are not stimulated always in the same ratio. Such a mechanism would account for the small size of the observed effects. Certainly the mechanism of analysis is far inferior to that of the mammalian ear, but would provide improved discrimination of biologically important noises from a background disturbance.

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HÆMATOLOGY

Mechanism of Clot Lysis

The availability of a large number of inhibitors of proteolytic enzymes, as well as the availability of highly purified streptokinase, plasminogen and plasmin, suggested to me the investigation of the nature of the enzyme or enzymes capable of dissolving fibrin clots. Proteolytic enzymes in general, but more particularly trypsin and chymotrypsin, are known for their ability to digest fibrin clots; certain snake venoms can also do this. The proteolysis of fibrinogen and fibrin by venoms, trypsin or plasmin appears to vary, depending upon which of the enzyme is used. The clotting of fibrinogen is the result of the splitting of an arginine peptide bond in the fibrinogen molecule[1]; this tends to produce a product (fibrin) which is much less susceptible to hydrolysis by trypsin and venoms than the parent substance, fibrinogen[2,3]. Fibrin, on the other hand, is as sensitive to plasmin as is fibrinogen[3].

I wish to report here some attempts made to distinguish a true fibrinolytic enzyme from other proteolytic enzymes which can also dissolve clots.

Fibrinolytic activity as defined by the ability of a substance to dissolve a clot is measured by noting the time required to dissolve a standard fibrin clot under specified conditions. Five-hundredths ml. aliquots of a solution containing various concentrations of the substance to be tested are mixed with 0·1 ml. portions of 0·4 per cent purified bovine fibrinogen[4] in 0·05 *M* veronal buffer of *p*H 7·4 and then to each sample is added 0·05 ml. of thrombin solution containing 10 units of thrombin per ml.; the clot formed in this mixture is kept at 37° C. in an incubator. The time required for lysis (complete dissolution) of the clot is noted in each case. The proteolysis of urea-denatured hæmoglobin has been carried out by the method of Anson[5] and the hydrolysis of synthetic amino-acid esters by the method of Troll *et al.*[6].

Table 1. Hydrolysis of Lysine Ethyl Ester by Streptokinase-activated Human Serum in the Absence and Presence of an Inhibitor, ε-Amino-Caproic Acid

	μM of lysine ethyl ester hydrolysed
Human serum	4·2
Streptokinase + human serum (incubated and then added to the substrate in the presence of amino-caproic acid)	18·6
Streptokinase + human serum + amino-caproic acid (incubated and then added to substrate)	3·4
Streptokinase + amino-caproic acid (incubated and then added to the substrate containing plasminogen (or streptokinase)	10·8

1 ml. of human serum was ten times diluted; to 1 ml. of this diluted serum, 1 ml. of streptokinase containing 1,000 units per ml. and 0·1 ml. of saline or amino-caproic acid are added. 0·2 ml. of this mixture was used in each experiment.

During the course of the experiments it was observed (Table 1) that a preincubated mixture of streptokinase and human plasminogen (that is, proactivator: in human blood the proactivator has been supposed, by some investigators, to be identical to human plasminogen) can hydrolyse synthetic amino-acid esters like lysine ethyl ester in the presence of ε-amino-caproic acid, although a preincubated mixture of streptokinase, plasminogen and the inhibitor (ε-amino-caproic acid) cannot do so. An appreciable amount of hydrolysis of lysine ethyl ester was, however, noted on the addition of streptokinase (or plasminogen) and ε-amino-caproic acid to a reaction mixture containing the substrate and plasminogen (or streptokinase). Similarly, hydrolysis of this synthetic substrate by plasmin, whether it is prepared from streptokinase-activated human plasminogen (serum) or after treatment of bovine plasma with chloroform or trypsin, is not inhibited by ε-amino-caproic acid. The results indicate that ε-amino-caproic acid can strongly inhibit the reaction of streptokinase with plasminogen to form an activator; once the activation process involving these two substances has occurred ε-amino-caproic acid cannot inhibit the hydrolysis of lysine ethyl ester any further.

As has previously been reported by Sarkar and Devi[3] I have also noted (Table 2) a very strong inhibition of clot lysis by ε-amino-caproic acid if streptokinase-activated human plasminogen (or serum) is used as a lytic agent; inhibition, to a much less extent, is observed if one uses purified plasmin prepared by any of the methods mentioned above. When the concentration of ε-amino-caproic acid is increased five-fold only about 25–30 per cent inhibition is noted. It should also be stated that the ability of streptokinase-activated human plasminogen to dissolve a clot far exceeds the ability of purified plasmin, no matter how the latter is prepared. Trypsin is a poor agent for lysing clot (Table 2). It seems quite likely, therefore, from what has been so far said, that neither plasmin nor trypsin are true fibrinolytic enzymes, although both of these enzymes ultimately can cause clot lysis, by virtue of their proteolytic activity. What I have termed a 'true' fibrinolytic enzyme is one which requires the same

Table 2. Effect of Amino-Caproic Acid on Clot Lysis by Streptokinase-activated Human Plasminogen and Plasmin prepared by Other Methods

	No inhibitor	ε-Amino-caproic acid (20 γ)
Streptokinase + human serum	4 min. 10 sec.	7–8 hr.
Plasmin (prepared from streptokinase-activated human serum)	7 min. 45 sec.	40–45 min.
Plasmin (prepared from chloroform-activated bovine serum)	14–15 min.	28–34 min.
Plasmin (prepared from trypsin-activated bovine plasminogen)	14–16 min.	25–30 min.
Trypsin	11–12 min.	15–16 min.

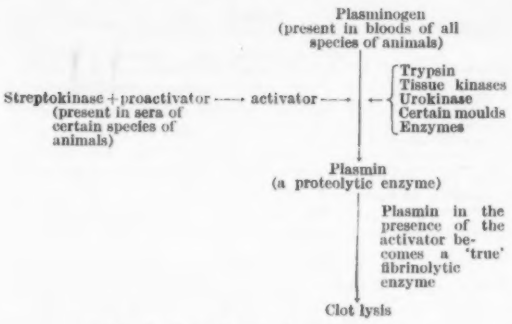

Fig. 1. General mechanism of clot lysis

time for complete dissolution of a fibrin clot and rendering fibrinogen unclottable by thrombin.

What then is the naturally occurring or 'true' fibrinolytic enzyme? Perhaps there is none. At least a single 'true' fibrinolytic enzyme is not known to-day. Plasmin, once thought to be the enzyme, does not, in fact, occur in the circulating blood. Its inactive precursor plasminogen, present in blood, is transformed to plasmin by an activator, which in turn is formed by an interaction of streptokinase with a proactivator found in the sera of certain species of animals (Fig. 1). Human blood contains this proactivator. It should be noted, however, that some investigators believe proactivator and plasminogen are not identical. Many mould extracts have been reported to be able to dissolve fibrin clot, but it was found by Grey and Sarkar[7] that these extracts dissolve a clot only by virtue of their tryptic activity. Thus it seems that no single substance (enzyme) qualifies at the present time as a 'true' fibrinolytic enzyme. Possibly plasmin, in the presence of the activator, acquires the property of a 'true fibrinolytic enzyme'. The reaction between streptokinase and human plasminogen proceeds with such extreme rapidity that as a rule there is little or no free streptokinase available in the system. This seems to exclude the possibility that streptokinase itself is involved in inducing fibrinolytic activity in plasmin. Whether or not the hypothetical activator of plasminogen itself is causing clot lysis, we do not know; although it looks as though it is the case. Recently, F. B. Ablondi and J. Hagan (personal communication) also expressed such a view.

Recently, Johnson *et al.*[8] demonstrated the inability of plasmin present in the circulating blood to dissolve an artificially formed intravascular blood clot. It was possible, however, to cause dissolution of the clot by introducing further quantities of streptokinase in the blood stream. Thus it appears from these experiments *in vivo* that it is not plasmin alone which dissolves the clot, but rather plasmin in presence of the activator (streptokinase + plasminogen) which does this.

In our attempt to define a 'true' fibrinolytic enzyme, we have mentioned that the ability of such an enzyme to dissolve a clot (clot lysis) and to render fibrinogen unclottable by thrombin should be nearly the same. Trypsin, as reported by Sarkar and Devi[3], needs a much longer time (20 times) to dissolve the clot than it requires to bring about fibrinogenolysis, whereas streptokinase-activated human plasminogen takes the same length of time for both fibrinolysis and fibrinogenolysis (Table 3). Reasons for the difference in the behaviour of these two different types of enzymes should be looked for in the mode of their actions. Enzymes like trypsin dissolve a clot by extensively degrading the protein fibrin. Trypsin also extensively degrades other proteins like denatured hæmoglobin, etc. The method for measuring proteolytic activity of an enzyme depends upon how extensively the enzyme has degraded the protein. In the case of streptokinase-activated human plasminogen it is probable that certain specific linkages holding the fibrin monomers together (to form the gel) are split. This explains why streptokinase-activated human plasminogen is equally active in causing clot lysis and in rendering fibrinogen unclottable by thrombin; whether or not this hypothesis is true is now under further investigation.

Table 3. The Ability of Streptokinase-activated Human Serum, Purified Plasmins and Trypsin to Dissolve a Clot and Render Fibrinogen Unclottable by Thrombin

	Time required for: Fribrinolysis	Fibrinogenolysis
Streptokinase + human serum	4 min. 10 sec.	4 min. 30 sec.
Plasmin (prepared from trypsin-activated bovine plasminogen)	14–16 min.	4–5 min.
Trypsin (25 γ)	11–12 min.	30–35 sec.

The work was carried out at the Institute of Laboratories, Boston, Mass., and financed by the Research Division of Jhonson and Jhonson, New Jersey.

A preliminary report of this work appeared in the Proceedings of the Seventh International Congress of Hæmatology held in London, Sept. 7–12, 1959.

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Lack of Hæmoglobin in a Fish

In the toad, *Xenopus laevis* Daudin, two specimens have been described completely lacking hæmoglobin[1,2]. I have been able myself to study a teleost fish without hæmoglobin, namely, an adult male of the cichlid *Cichlasoma severum* (Heckel).

The fish, which measured 72 mm. in length, had lived for about two years in a large tank (25 ± 1° C.), was less active than other cichlids of the same litter and during the last few months mostly moved in the surface of the water layer. In this period only little food was taken. The animal became much emaciated, its response to external stimuli almost ceased and ultimately it was killed by decapitation. The animal was smaller than the fishes of the same brood, of which the length varied from 109 to 154 mm.

At autopsy the blood vessels appeared to be white or perfectly colourless except for the chromatophores in their walls. The heart was pale cream and the liver grey. The gills and the kidneys were cream. The gall bladder was enlarged and contained a large quantity of dark green bile pigment. The spleen was enlarged and coloured light brown. The examination of the blood smears showed that hæmoglobin

was not identifiable. Erythrocytes were present, however.

The histological investigation showed that the structure of the organs was normal.

On the strength of accumulation of dark green bile pigment, which was also stated in the case of Ewer[2], it may be concluded that the extensive destruction of the hæmoglobin had occurred very recently.

Another point of correspondence with the case of Ewer was the enlarged light brown spleen which, unlike the case of De Graaf[1], was not coloured slightly yellowish-white.

According to De Graaf, his animal without hæmoglobin had been in that condition all its life, with the implication that the growth to maturity in natural conditions is possible without the presence of hæmoglobin. Ewer, however, arrived at a different interpretation, namely, that the total anæmic condition is a pathological state, which may originate after the adult has become mature. My case, in which also the hæmoglobin destruction had only just been completed, is an argument for Ewer's concept.

Survival without hæmoglobin is distinctly possible, which, however, by no means implies that an animal without hæmoglobin can be as active as a normal one. In my specimen the latter state could be clearly distinguished.

According to De Graaf, normal *Xenopus laevis* are capable of functional elimination of at least 80 per cent of their hæmoglobin by carbon monoxide treatment.

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Activation of Plasminogen by Staphylokinase

Some animal plasminogens, which are unaffected by streptokinase alone, are activated by streptokinase and human globulin. Müllertz[1] has postulated the existence of a proactivator in human serum. Staphylokinase, without human globulin, activates a wider range of animal plasminogens[2] and may, therefore, not require proactivator.

Staphylokinase was prepared from the supernatants of fibrinolytic strains of *Staphylococci* shaken for 7 hr. The supernatant was heated at 75° C. for 30 min. Some inert protein was precipitated at *p*H 3·3. After dialysis, staphylokinase was precipitated at *p*H 4·2.

Euglobulin, in the original serum volume, was used as a source of animal plasminogen. Human plasminogen, prepared by the Kline procedure[3], provided proactivator. Plasmin was assayed by the caseinolytic method described by Norman[4], perchloric acid being used instead of trichloracetic acid.

0·2–0·3 ml. of euglobulin was incubated with up to 400 units streptokinase ('Dornokinase', Burroughs Wellcome and Co.) or an equivalent amount of staphylokinase (assayed against human plasminogen), and with or without 3×10^{-3} units human plasminogen. Maximal activity was obtained after 5–10 min. with 20–140 units kinase. Bovine euglobulin did not inhibit the activation of human plasminogen by staphylokinase.

Table 1

	Human	Guinea pig	Rabbit	Bovine
Streptokinase	+	−	−	−
Streptokinase + Proactivator	+	+	+	+
Staphylokinase	+	+	+	−
Staphylokinase + Proactivator	+	+	+	−
Plasminogen (units × 10^{-3} per ml. serum)	40	57	34	28

The results, which are shown in Table 1, indicate that staphylokinase does not act through proactivator.

A detailed report of this work is being prepared.

I wish to acknowledge the gift of Fraction III of human plasma from E. R. Squibb and Sons, by courtesy of the American National Red Cross.

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PLANT PHYSIOLOGY

Abnormal Growth and Development in Pea resulting from Exposure to Adverse Conditions during Germination

Kidd and West[1] showed that the amount of growth made by a plant could be determined by the conditions to which the germinating seed was exposed. In their investigations they measured the yield obtained from plants grown from seed soaked in water for varying lengths of time, and they found that in most cases of extended soaking, though the seed germinated more rapidly than seed planted directly in moist soil, the yield obtained from such seedlings was reduced. Their observations of 'physiological predetermination' have been carried further by examining the effect of soaking peas (*Pisum sativum* L.) in water. With this species when seeds are soaked in water for 48 hr. the seedlings that eventually develop may be abnormal (Fig. 1). Normally a small number of seeds, 200, is soaked in a large volume, 500 ml., of tap water kept at 20° C. in darkness. The depth of water covering the seeds was 15 cm., and

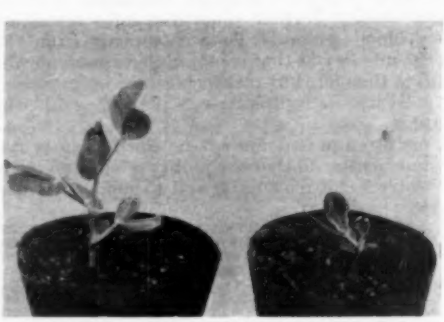

Fig. 1. The plant on the right is a seedling grown from seeds soaked in water for 48 hr. before planting. That on the left is the control planted directly in moist soil

the soaking can best be done in 500-ml. Erlenmeyer flasks.

The effects observed may be related to one or more of the following conditions; (*a*) A disturbance of the normal metabolism during the first 48 hr. of germination and the maintenance of this abnormal condition during the first stages in development. (*b*) The removal by leaching of an essential water-soluble metabolite. (*c*) The accumulation within the seed of a material which adversely affects growth.

It was thought that peas soaked in stagnant water would respire anaerobically, and therefore it was decided to compare the response of soaked seed with seed which were exposed during the first 48 hr. of germination to an atmosphere containing 20 per cent carbon monoxide. The seeds which were exposed to this atmosphere were kept in darkness, at 20° C., during the period of exposure. In these seeds normal respiration would be blocked since the cytochrome system would be inoperative in this atmosphere. To determine if metabolites were lost, or substances accumulated during soaking, a third sample was kept in running tap-water for 48 hr. At the start of the experiment a fourth sample was planted directly in moist soil in an unheated greenhouse. At the end of treatment the other three samples were sown out in the same bed. After 23 days the plants were harvested, and measurements made immediately on a sample of 30 plants from each treatment (Tables 1 and 2). The number of nodes formed by the largest bud of the first and second nodes (in pea there are usually more than one axillary bud at each node) and the condition of the terminal bud were recorded. If flower primordia were present the number of these was noted, but only when the primordium had recognizable flower parts present; if no flower buds were present the apex was scored as alive and active, or dead. The remainder of the seedlings produced were stored in 70 per cent alcohol, and from them was obtained the length of the largest axillary bud at the first and second node, and the length of the largest flower present. Gross abnormalities were treated separately. In the batch planted directly into moist soil 161 seedlings were present at harvest and of them 7 were grossly abnormal, while seeds which had been exposed to carbon monoxide produced 171 seedlings with 9 abnormal. Those seeds which were exposed to water produced respectively 129 and 175 seedlings with 34 and 5 abnormals for those soaked in stagnant and running water. The most common type of aberration encountered is suppression of the terminal bud and development of the basal axillary buds. Leaf shape is affected and treated plants are usually slightly chlorotic.

The findings are recorded in Tables 1 and 2.

The results indicate that the normal course of development in pea can be altered by exposing the seed during germination to conditions which affect aerobic respiration. This effect is seen as the removal of apical dominance, in extreme cases by the death of the terminal bud. It appears that the tissues most affected by the treatment are the meristems present in the embryo.

This work is being continued to determine the nature of the changes which take place in seeds germinating under the conditions described.

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Table 1

	No. of plants with apical buds			Total No. of formed flowers	Average No. of nodes	
	Flowering	Veg.	Dead		Bud No. 1	Bud No. 2
Moist soil	28	1	1	75	2·86	3·76
Running water	28	1	1	49	1·30	3·23
Stagnant water	18	4	8	0	3·50	4·42
20 per cent carbon monoxide	25	1	4	40	1·83	3·24

Table 2

	No. of plants	Average length (relative to moist soil = 100)					
		Bud No. 1		Bud No. 2		Largest flower	
Moist soil	131	5·4	100	9·1	100	5·6	100
Running water	145	5·7	105	9·7	106	5·0	89
Stagnant water	99	6·6	122	11·2	124	3·0	54
20 per cent carbon monoxide	141	6·0	111	9·8	108	2·8	50

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Nitrate Content of Herbage at Different Manurial Levels

FOLLOWING on the results reported in *Nature*[1], nitrate nitrogen determinations have recently been made on herbage samples provided by Dr. Rice Williams, of the National Agricultural Advisory Service, from an experiment where sulphate of ammonia had been used at six levels, 0, 2, 4, 6, 8 and 12 cwt. per acre, to swards consisting of a number of different grass mixtures[2]. Nitrogen was applied in mid-April and the herbage was cut six weeks later. The results from one of these mixtures (mixture *B*) are illustrated in Fig. 1. Mixture *B* was seeded down with Italian ryegrass, perennial ryegrass *S*.101, timothy *S*.48, cocksfoot *S*.26, *S*.143, *S*.37 and Danish, red clover *S*.123, alsike, white clover *S*.100 and *S*.184. The experiment was in the form of a randomized block, each level of application having three replicates.

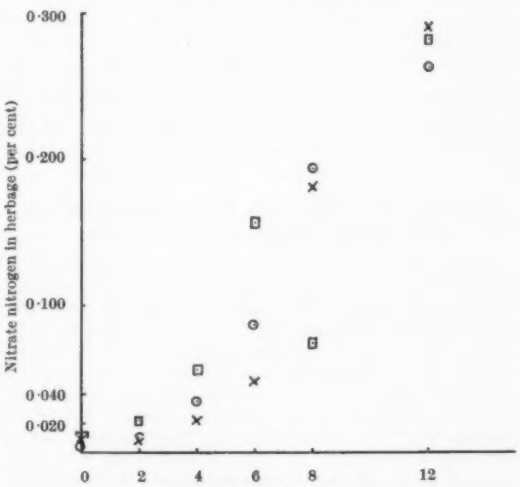

Fig. 1. Relation between levels of nitrogen application and of nitrate nitrogen in herbage. ○, ⊡, ×, replications of each treatment

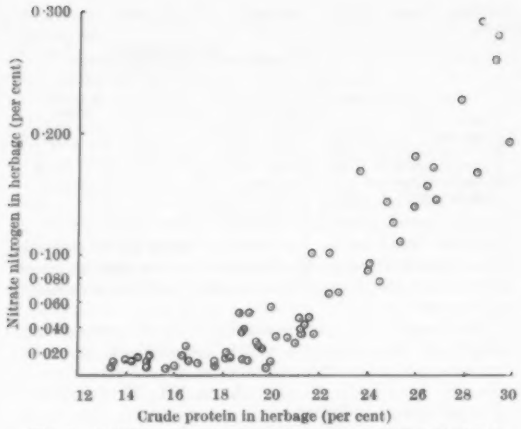

Fig. 2. Relation between percentage crude protein and nitrate nitrogen in herbage

It is seen that nitrogen, applied in the ammonium form, and with a normal interval between application and cutting, has resulted in accumulations of nitrate nitrogen detectable at the 4-cwt. level and considerable at the 8- and 12-cwt. levels.

In Fig. 2, nitrate nitrogen is plotted against crude protein; results from two other grass mixtures in the same experiment are also included. I am indebted to Dr. Rice Williams for the crude protein data.

In amounts greater than 0·07 per cent of the dry matter, expressed as nitrogen, nitrate is reported to be toxic to the animal[3], and amounts greater than 0·22 per cent are reported to be lethal[4]. In the present experiment a crude protein content greater than about 22 per cent would render the material suspect for feeding purposes.

Full details of this investigation are being prepared for publication and will appear elsewhere in due course.

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Influence of Hydrogen Ion Concentration and Autoclaving on Gibberellin

In at least two reports the method of sterilization for medium to be used for tissue culture experiments was autoclaving[1,2]. The question of the heat stability of gibberellin is raised. It is generally thought that gibberellin is stable on the basic side of neutrality and at room temperature at neutral or near neutral *p*H, and more labile at elevated temperatures at extreme *p*H values. It has been stated that even weakly acid media will destroy gibberellin and that it is much more stable in neutral and basic solutions (Stowe, B. B., private communication, November 7, 1958).

Several investigators have recently been interested in the heat stability of gibberellin in culture media in the *p*H range 5–6. Experiments have generally been conducted with gibberellin by the sterile-filtration technique. The need for this technique and validity of autoclaving with the medium have been investigated.

Treatments were carried out with autoclaved and unautoclaved stock solutions of gibberellin (supplied by Chas. Pfizer and Co., and consists of gibberellin A and gibberellin X, gibberellic acid) at 100 μgm. per ml. The solutions were buffered to maintain a stable *p*H during autoclaving and treatment of the plants. The buffers at *p*H 1·0 and 3·5 were phthalate–hydrochloride mixtures; *p*H 6·0 was a phthalate–sodium hydroxide mixture; *p*H 10·0 was a boric acid–potassium chloride–sodium hydroxide mixture[3]. Autoclaving was at 20 lb./sq. in. for 15 min.

In all cases the solutions were cooled after autoclaving and placed in the refrigerator for storage before and after use on the plants. During the total length of the experiments (January 17 to December 5, 1959) new stock solutions were made up and new sets of solutions autoclaved for use on the test plants. The solutions, which were re-adjusted to *p*H 6·0, were first autoclaved at the indicated *p*H values and after cooling were adjusted with hydrochloric acid or sodium hydroxide to a *p*H of 6·0 before treatment (0·05 c.c. of the solution) of the plant.

These experiments were set up using the Phinney[4] test for dwarf-1 mutant corn. The plants were treated one week after germination. The dosage was 5γ (0·05 c.c. of 100 γ/ml.) per plant treated only once, at the beginning of the experiment. Recorded readings were taken on the plants two weeks after treatment.

To test whether the *p*H or buffer solutions alone had any effect on growth, the dwarf mutants received likewise 0·05 c.c. of the respective buffer solutions. Measurements of the second internode only were taken at the end of two weeks from treatment. Three plants were used in each pot for each treatment. Results were taken from four to five separate experiments over a 4-month period.

From Table 1, the following observations can be made: (1) all autoclaved solutions possessed less activity than those unautoclaved: (2) the highest activity was from solutions buffered at *p*H values of 6·0 and 3·5, for all treatments, with very little difference between the two; (3) the least activity was from solutions at *p*H 1·0 for all treatments; (4) activity for *p*H 10·0 was intermediate between that at *p*H 3·5 and 6·0, and 1·0; (5) plants treated with buffer alone showed no stimulation whatsoever, being

Table 1. Treatment of Dwarf-1 Mutant Corn Seedling, with 5 μgm. of Gibberellin at Various Buffered *p*H Values, after Autoclaving or not Autoclaving

Measurement of the second internode in centimetres after two weeks treatment; numbers in brackets are number of plants included to calculate average

Treatment	*p*H of buffer			
	1·0	3·5	6·0	10·0
Unautoclaved	2·5±1·2* (12)	6·8±2·0 (15)	6·6±1·4 (12)	5·2±1·4 (11)
Autoclaved	1·3±0·4 (10)	4·6±1·5 (14)	4·9±1·8 (12)	3·3±1·1 (12)
Autoclaved, readjusted to *p*H 6·0 after autoclaving	1·8±0·6 (10)	4·6±0·9 (13)	4·5±1·3 (15)	3·3±1·4 (11)
*p*H control	1·0 (3)	1·2 (3)	1·5 (3)	1·0 (2)
Normals	5·5±2·3 (22)			
Dwarf controls	1·2±0·4 (12)			

* Standard error of the mean.

the same as the dwarf controls; (6) solutions initially autoclaved in the various buffers and afterwards adjusted to a common *p*H of 6·0 were uninfluenced by this post-autoclaving treatment; (7) all gibberellin solutions, regardless of type of treatment, showed greater activity than solutions containing no gibberellin (*p*H control plants), and caused greater growth of the dwarfs than the untreated (dwarf) controls; (8) the unautoclaved gibberellin solutions at *p*H 3·5 and 6·0 showed greater activity than the normal, non-dwarf plants; (9) the reduction in activity of gibberellin due to autoclaving was in no case greater than 50 per cent (for *p*H 1·0) and for solutions at *p*H 3·5 and 6·0 it was roughly 33 and 25 per cent, respectively.

From these observations one may draw the following conclusions: (1) There is significant (statistical) loss of activity caused by autoclaving of gibberellin, but this loss is not so significant biologically (see explanation below); (2) the loss of activity is between one-third and one-fourth of the original activity at the optimum *p*H value for most culture solutions employing gibberellin, especially sterile tissue culture; (3) based on the experiments with *p*H controls and the re-adjusted autoclaved solutions, the *p*H factor itself does not influence these plant responses directly; the effect of heat and *p*H is rather on the gibberellin molecule itself, and subsequent influence of the latter on plant response.

The general over-all conclusion is that the autoclaving of gibberellin at the normal *p*H of culture media is not biologically significantly detrimental or destructive to the gibberellin content in the medium. From standard curves of biological activity, as well as response in plant tissue culture, the loss of as little as one-third to one-fourth, or even more, of the activity of gibberellin at any single concentration is never very significant, since most experiments employ the logarithm of the concentration of growth factors instead of linear units. Autoclaving of other organic growth factors and auxins, especially indoleacetic acid, would show approximately similar losses. Therefore, it is generally safe to use the autoclaving technique in the usual experiments employing gibberellin in plant tissue culture, especially where the amounts employed are greater than 1 p.p.m.

Since these conclusions are based on one of the only reliable methods for the assay of gibberellin at present—the bioassay technique, limited to the assay with Dwarf-1 mutant corn in this instance—it is not possible to speculate what the active compound(s) is (are). It is specifically adapted to each bioassay test. Further work, both biological and chemical, is required to identify the active principle.

I wish to thank Chas. Pfizer and Co., Inc., for supplying the gibberellin, and the National Science Foundation for supporting the investigation. Mr. Clarence Saulsberry assisted in the experimental work; Dr. B. O. Phinney supplied the Dwarf-1 mutant seeds.

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RADIOBIOLOGY

Effectiveness of Dietary Substances in reducing the Retention of Chronically Ingested Radiostrontium; Studies with Tannin

THERE has been considerable interest in the testing of substances that may reduce the body burden of chronically ingested radiostrontium. The present work, using tannin as an example, emphasizes the caution that must be used in the interpretation of single-dose studies, and also describes a relatively short-term procedure which appears to be practical.

In a recent report, Ukai *et al.*[1] have shown that the skeletal retention of a single dose of strontium-90 could be reduced if followed immediately by the oral administration of a 1 or 2 per cent tannin solution. It has been suggested from these results that consumers of tannin (in tea) would absorb and retain less fall-out strontium-90 than otherwise. Such interpretations of data from single-dose studies applied to situations of normal strontium-90 ingestion can be especially misleading. First, strontium-90 is ingested continuously as a contaminant in most food products; secondly, strontium-90 is consumed simultaneously with dietary calcium and other constituents of the diet. Under these conditions, a complexing agent may yield an entirely different effect from that when it is given as a single dose with carrier-free radiostrontium. In fact, our previous experience has shown that substances which complex or chelate strontium and calcium, for example, citrate, phytate, sodium ethylenediaminetetraacetate, were without effect in reducing the body burden of continuously ingested radiostrontium[2]. In view of this prior knowledge, it was felt necessary to determine the influence of tannin on radiostrontium and radiocalcium retention in the situation where (*a*) the radiostrontium is continuously ingested over a period of days, (*b*) the tannin is consumed over the same time period, and (*c*) the normal constituents of the diet are also present.

Twenty-four rats were divided into four groups of six rats each and placed in individual cages. Drinking-water labelled with essentially carrier-free calcium-45 and strontium-85 was made available in graduated drinking tubes; the levels of calcium-45 and strontium-85 were 0·1 and 0·01 μc. per ml., respectively. At the same time, the rats were given a complete semi-synthetic diet containing either 0, 1, 2 or 4 per cent tannin (Nutritional Biochemicals, Inc.); the level of calcium in these diets was about 0·48 per cent. The rats were allowed to ingest the 'spiked' water and diet *ad libitum* over an experimental period of ten days. The amount of water and diet consumed was measured. At ten days, the rats were killed and retention of calcium-45 and strontium-85 in the femur was determined by usual radioassay procedures. The results are given as 'per cent of total ingested activity'. It should be pointed out that previous studies have shown that radiostrontium and radiocalcium ingested continuously in drinking water equilibrate with, and act similarly to, these elements ingested in the diet[3].

The results are presented in Table 1. It may be seen that the presence of tannin in the diet at the higher levels appreciably decreased the growth-rate of the experimental animals although feed consump-

Table 1. INFLUENCE OF TANNIN ON THE FEMUR RETENTION OF CONTINUOUSLY INGESTED CALCIUM-45 AND STRONTIUM-85

Group	Concentration of tannin in diet (per cent)	Body-weight*			Feed intake* (gm.)	Femur retention of radionuclides†		OR‡
		Initial (gm.)	Final (gm.)	Gain (gm.)		^{45}Ca (per cent ingested dose)	^{85}Sr (per cent ingested dose)	
1	0	235	261	26	143	2·3 ± 0·3	0·46 ± 0·03	0·20 ± 0·01
2	1	237	257	20	174	2·3 ± 0·2	0·58 ± 0·08	0·25 ± 0·02
3	2	243	262	19	159	2·1 ± 0·1	0·66 ± 0·06	0·30 ± 0·02
4	4	239	242	3	159	2·0 ± 0·1	0·64 ± 0·03	0·32 ± 0·04

* Body-weight and feed intake given over 10-day period.
† Values represent mean ± standard error of the mean of six animals per group.
‡ Observed ratio (OR) = ^{85}Sr/^{45}Ca in femur ÷ ^{85}Sr/^{45}Ca in diet.

tion was not reduced. In regard to radionuclide retention, a slight decrease in radiocalcium retention by the rat femur was noted in the tannin groups in contrast to the controls. However, in the presence of 2–4 per cent dietary tannin, the strontium-85 content of the rat femurs was significantly increased, causing an increase of the strontium/calcium observed ratio. An increased strontium/calcium ratio had similarly been observed in rats fed a liquid milk diet containing sodium ethylenediaminetetraacetate. Since tannin and ethylenediaminetetraacetate possess the common property of binding calcium ions to a somewhat greater degree than strontium ions, the present results may possibly be explained as follows. Radiostrontium previously complexed with tannin in the gut could be replaced by stable calcium and, therefore, become available for absorption. Parental tannin would act similarly, that is, releasing complexed strontium-85 when replaced by plasma calcium.

The above results are not in direct conflict with those of Ukai *et al.*[1] because entirely different conditions were employed in the two studies. Any disagreement would be in the extrapolation of single-dose data to the chronic situation in which strontium-90 is ingested with the diet at each meal. When this chronic situation is experimentally simulated as in the present study, it was observed that tannin at various levels in the diet had *no* beneficial effect in reducing the body burden of radiostrontium in the rat. Although single-dose studies of the type referred to may have usefulness in readily assessing the potential value of any test substance, it is recommended that promising compounds should be subjected to a chronic ingestion test before extrapolations are made to the chronic situation. It is further suggested that the influence of the test substance should be simultaneously determined on radiocalcium retention, since interpretations are facilitated and important information of possible effects on an essential nutrient is thereby provided.

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Early Injury of Chromoexcretion after Total Irradiation of Rats

IT is claimed by all available literature that damage occurs to the function of the liver after whole-body irradiation by doses, approaching *LD*100, from as late as the stage of development of the secondary post-radiation changes[1,2]. Some biochemical results, however, support the opinion that the liver cell should be damaged in its function at the earliest stage of an acute irradiation disturbance[3–5]. To prove the early functional lesion we carried out experiments with bengal rose tagged with radioactive iodine-131.

Experiments were performed on 50 male rats of the Wistar strain averaging 200 gm. in weight. Twenty-six rats were irradiated with a dose of 600 r. by the deep X-ray apparatus of 200 kV., 15 m.amp., filtration 3 mm. aluminium at a distance of 75 cm. and 32 r./min. The remaining 24 rats were used as a control group. Tests were accomplished in 4 groups, of 6 and 8 rats respectively, the controlled and irradiated ones, 2, 6 and 24 hr., and 14 days after the irradiation. At the given intervals we applied to the tail vein of the rats 5 μc. bengal rose–iodine-131 in 1 ml. of isotonic solution[6]. 10 min. after the injection the rats were killed, the liver was taken out and homogenized separately.

Gamma activity of the homogenates was determined by the scintillation method. The activities of the control-group homogenates were taken as 100 per cent and the activities of the irradiated groups were expressed as a percentage of the control-group activity.

In the group tested 2 hr. after the irradiation the uptake value of 81 per cent, as compared with 100 per cent of the control group, was still above the 5 per cent limit of significance. The further group, tested 6 hr. after irradiation, has its uptake lowered to 83 per cent of limit of error below 1 per cent. The group killed 24 hr. after irradiation has its uptake lowered to 76 per cent with 0·5 per cent limit error, and that killed on the fourteenth day after irradiation exhibits lowering to 74 per cent with 1 per cent significance.

Uptake of bengal rose is a specific property of polygonal liver cells. Radioactive bengal rose permits differentiation of the great damage done to the blood—or bile pole of the liver cell. In preliminary experiments, during investigations for the most suitable moment for homogenization after injection, we ascertained the maximum difference in the tenth minute after the application of colouring matter, that is, at the uptake maximum. This fact is an indication of considerable damage caused to the blood pole of the liver cell. The question of this mechanism is still open, and is the subject of further investigation.

The possibility of distributive volume changes of bengal rose is not likely to make itself felt to any extent in these results. This is due to the fact that distributive volume for bengal rose is practically equal to the plasma volume, and there is no literature known to us suggesting that considerable changes occur in the plasma volume in the early stages after the irradiation of the whole body.

We believe that the significant lowering of uptake maximum in the sixth hour after irradiation explains the early injury to the chromo-excretional function in rats after whole-body irradiation by lethal doses of 600 r. using bengal rose–iodine-131.

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BIOLOGY

Thermal Barrier to the Infectivity of *Entamœba invadens* in Snakes

THE optimum temperature for the *in vitro* growth of *Entamœba invadens* has been determined by several investigators to be between 20 and 30° C.[1,2]. I found that the maximum temperature at which *E. invadens* could be grown in developing chicken embryos was 30° C.[3]. The following account represents the results of a preliminary investigation on the ability of *E. invadens* to establish itself in snakes kept at temperatures above normal.

Three adult grass snakes, *Thamnophis sirtalis*, free of parasitic Amœbæ, were used in each of the two experiments. All the snakes were inoculated *per os* with equal doses of a heavy suspension of trophozoites and cysts of the *I.P.*2 strain of *E. invadens*[4], taken from polyxenic cultures.

In the first experiment snakes 1 and 2 were placed in individual jars in a hot room, in which the temperature fluctuated between 34° and 37° C. Snake 3 was kept in the laboratory, the room temperature varying from 20° to 23° C. During the course of the experiment the snakes' fæces were examined for the presence of Amœbæ and of blood, which is an indication of intestinal ulceration produced by the Amœbæ. The snakes' rectal temperature was recorded at the same time by means of a very fine thermometer. Table 1 represents the findings in Exp. 1.

Three other snakes were similarly inoculated in the second experiment; Nos. 1 and 2 were placed in separate jars in the hot room and No. 3 was left in the laboratory.

Snake 1 died two days after inoculation. Upon autopsy Amœbæ were not seen in its intestine or liver, but a culture made from the intestinal contents became positive for *E. invadens*.

Table 1

	Days after inoculation	Room temperature (deg. C.)	Rectal temperature (deg. C.)	Microscopical examination of fæces
Snake 1	1	35·5	34·5	Negative
	2	37	32	Negative
	4	34	34	R.B.C., no Amœbæ
	5	35·5	34·5	R.B.C., no Amœbæ
	6	35	33·5	No Amœbæ
	7	34·5	34	No Amœbæ
	8	Died. No pathological changes and no Amœbæ seen in internal organs.		
Snake 2	1	35·5	34·5	Negative
	2	37	32	Negative
	4	34	34	R.B.C., no Amœbæ
	5	35·5	34·5	R.B.C., Amœbæ present
	6	35	34·5	Few Amœbæ
	7	34·5	34·5	Few Amœbæ
	8	Died. No pathological changes and no Amœbæ seen in internal organs.		
Snake 3	1	21	20	Negative
	2	22	22	Negative
	4	20	20	Negative
	5	20·5	19·5	Blood and Amœbæ
	6	21·5	21	Blood and Amœbæ
	7	23	25	Blood, no Amœbæ
	8	Killed. Large intestine hæmorrhagic and ulcerated. Amœbæ recovered in cultures made from the intestine and liver.		

On the seventh day after inoculation the rectal temperature of snake 2 was 33° C., while that of the room was 34·5° C. There were no living Amœbæ in its fæces on that day, but many cells resembling dead Amœbæ were observed. A sample of fæces was taken from the same snake on the fifteenth day after inoculation, but no Amœbæ were seen in it, nor did the cultures made from the fæces become positive for Amœbæ. Snake 2 was found dead on the seventeenth day after inoculation. There were no pathological changes in its intestine or liver. Cultures made from these organs did not become positive for Amœbæ. It was also noted that the flagellates, which were very numerous in the intestine of this snake at the beginning of the experiment, were all gone when autopsy was performed.

Snake 3, which was kept in the laboratory, developed typical amœbiasis about a week after inoculation and was killed on the tenth day. Its large intestine was heavily ulcerated, and *E. invadens* were seen in the intestine and the liver.

These preliminary experiments have shown that *E. invadens* is unable to establish infections in snakes at high temperatures, although, as seen in snake 2 in Exp. 1 and in snake 1 in Exp. 2, the Amœbæ survived in the intestine for a few days. It is also interesting that the flagellates, often present in snakes' intestines, apparently could not survive at high temperatures. The snakes kept at high temperatures died within relatively short periods of time, although their death was not due to the amœbic infection.

It is planned to repeat these experiments, using strains of *E. invadens* which have been adapted to *in vitro* growth at 35° C.

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Variations in the Plasma-Level of Chloride in Hatchery-reared Yearling Atlantic Salmon during Parr–Smolt Transformation and following Transfer into Sea-Water

THE successful adaptation of juvenile Atlantic salmon to sea-water requires a prior physiological 'metamorphosis'—parr–smolt transformation[1]. The occurrence of this change appears to depend in part upon age, and in part upon the complex of factors controlling the growth-rate of the parr[2]. In addition to external evidences of parr–smolt transformation such as loss of parr marks, decrease in condition factor and deposition of guanine there must also be some variation in biochemical systems associated with the regulation of body electrolyte-levels relative to those of the environment. Evidence for such changes may be seen in the changing plasma chloride-levels of two migratory salmonids, *Oncorhynchus masou* and *Salmo gairdneri*, during transition from parr to smolt stages[3]. Several investigators have also reported marked development of Keys–Willmer cells, units thought to have an ion secretory role, in a number of species of salmon prior to downstream migration[4]. Fontaine, however, could find no significant variation in blood chloride-levels of smolting Atlantic salmon, although a decrease did occur in tissue concentration[5].

During the course of an investigation of factors influencing the adaptability of hatchery-reared yearling Atlantic salmon to sea-water it was possible to observe plasma chloride-levels in fish maintained in freshwater over a five-month period. The animals were obtained from the Grand Lake Fish Culture Station, Nova Scotia, and were held in recirculating aquaria at 11° C. in the laboratory. Analysis of chloride content was carried out by the mercurimetric titration procedure on 50 and 100 lambda-plasma samples. Samples were obtained by exposed cardiac puncture from anæsthetized animals.

Fig. 1 summarizes results obtained on the 45 animals sampled. These were assessed at the time of sampling as parr (parr marks distinct, no silvering), silvery parr (parr marks more or less distinct, some silvering) or smolt (parr marks absent, marked silvering). In small parr (6–15 gm.) chloride-levels were relatively size-stable and ranged from 125 to 139 m*M*/l. In somewhat larger parr (15–26 gm.) plasma chloride decreased markedly with increase in weight. In silvery parr (17–31 gm.), on the other hand, chloride concentrations increased with increases in weight to a maximum of 145–150 m*M*/l. A slight decrease from this level was observed in the smallest smolt sampled, but values for larger animals were relatively constant at between 130 and 140 m*M*/l.

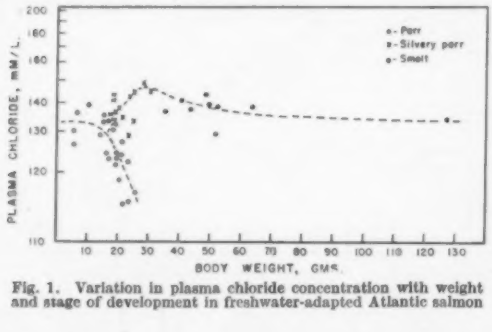

Fig. 1. Variation in plasma chloride concentration with weight and stage of development in freshwater-adapted Atlantic salmon

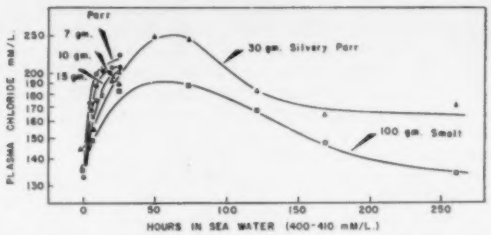

Fig. 2. Plasma chloride concentrations of parr (7, 10, 15 gm.), silvery parr (30 gm.) and smolt (100 gm.) following transfer from freshwater into sea-water (chloride concentration: 400–410 m*M*/l.)

From the observations it is inferred that the initiation of parr–smolt transformation is accompanied by alterations in the electrolyte metabolism of the parr which lead to a loss in regulatory ability. Salt balance in freshwater fishes involves the precise adjustment of uptake processes (dietary gain, active absorption) with processes leading to loss or dilution (urinary output, outward diffusion). A predominance of the latter group of factors is indicated in late parr, while a reversal of this effect is apparent in silvery parr. The results suggest, as well, that the process of smoltification may be well under way before any obvious indications of its occurrence are present, since chloride imbalance was present in parr displaying distinct parr marks and the absence of any silvering.

Variation in patterns of endocrine activity may account for the distinct decrease in regulatory efficiency which is apparent in the early stages of parr–smolt transformation. Data assembled by Pickford and Atz and by Hoar[6] suggest that increased pituitary, thyroid and adrenal cortical activity accompany smoltification. Of particular interest are the demonstrations by Hoar[4] of a relationship between thyrotropic hormone and the development of Keys–Willmer cells in Atlantic salmon parr, and by Fontaine and Hatey[7] of marked increases in the blood-levels of 17-hydroxycorticosteroids in the smolt stages of the same species.

Chloride-levels of fish transferred from freshwater directly into sea-water (400–410 m*M*/l.) are recorded in Fig. 2. Values were interpolated from regression equations relating plasma chloride to body-weight in groups of 15–20 fish.

Small parr (7, 10, 15 gm.) took up chloride rapidly and none survived for longer than 26 hr. Smaller parr took up chloride more rapidly than did larger animals, and died earlier. This observation is consistent with those made earlier by Huntsman and Hoar[1] on the same species.

Animals in the process of transformation appeared to be developing the capacity to become adapted to sea-water. Increases in chloride-level were, however, more marked than those observed in smolt, and the silvery parr required a longer time to return to freshwater chloride-levels than did completely transformed fish. The process of adaptation to sea-water required about ten days in fully transformed smolt.

In general, this study tends to support the conclusions of Koch, Evans and Bergstrom[8] based upon sodium regulation in Atlantic salmon parr and smolt. A loss of regulatory capacity occurs while the fish become transformed from the freshwater-adapted parr stage to the potentially marine smolt stage, while adaptation to sea-water appears to be dependent upon both size and stage.

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Study of Life-cycle of *Schizosaccharomyces octosporus* by means of Ultra-thin Sectioning and Electron Microscopy

CYTOLOGICAL studies of the yeast of the genus *Schizosaccharomyces* have been few and limited primarily to observations by means of light microscopy[1–3]. Although these studies reveal the nature of some of the general cytological changes which occur during various phases of the life-cycle of these yeasts, detailed studies are lacking. Some of the conflicting views and limited observations of these investigators may be attributed at least in part to the resolution limit of the light microscope. A study of the nature and sequence of the cytological changes which occur during cell division, conjugation, ascosporogenesis, and germination was therefore carried out by means of ultra-thin sectioning and electron microscopy in order to obtain a more detailed and accurate description of the cytological changes which occur. Various cytochemical methods were also employed in order to correlate structures observed in electron micrographs with structures observable with the light microscope. *Schizosaccharomyces octosporus*, N.R.R.L. *Y*-854, obtained from Dr. L. J. Wickerham, was selected for study. The techniques used for specimen preparation have been described previously[4].

Fig. 1,*a–i* illustrate the nature and sequence of the cytological changes accompanying cell division. It was observed that karyokinesis occurs well in advance of cytokinesis and that transverse cell-wall formation occurs by the annular centripetal growth of an inner lateral portion of the cell wall. The cytoplasmic membrane appears to remain in close proximity to the cell wall during cytokinesis. After formation the transverse cell wall increases in thickness and electron-dense membrane-like structures are formed. The transverse wall then splits as shown, the transverse membranes serving initially as the outer portion of the cell wall. These membranes may be analogous to the splitting plate observed in dividing cells of *Histoplasma*[5]. Nuclear division appears to occur by a process of elongation and constriction, further observation of chromatin behaviour being beyond the scope of the techniques employed. The nuclear membrane appears to remain intact throughout all the observed stages of nuclear and cytoplasmic division.

The conjugation process (Fig. 1,*j–o*) appears to be initiated by the attachment of cells in pairs by a

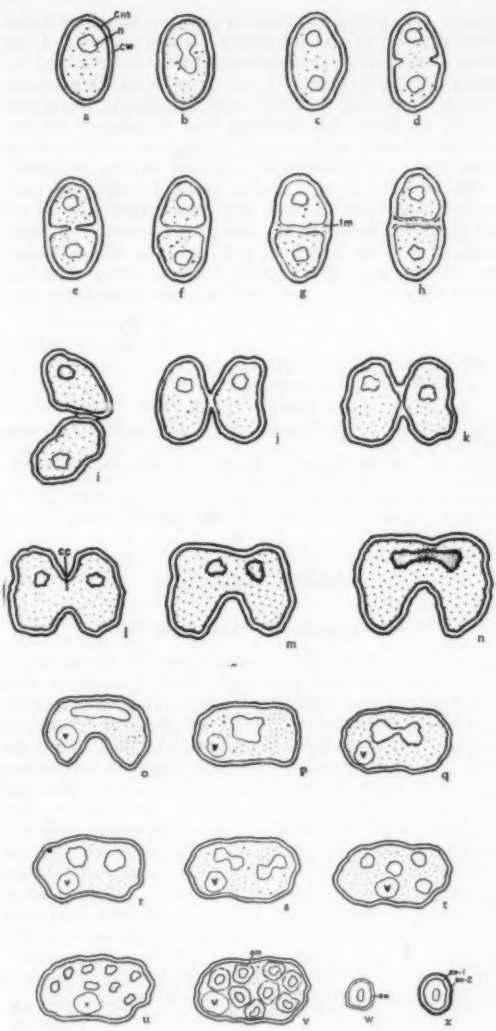

Fig. 1. Life-cycle of *S. octosporus*. *a–i*, Cell division; *j–v*, conjugation, nuclear division and sporulation; *w*, developing ascospore; *x*, appearance of a mature ascospore prior to germination. *AM*, Ascospore membrane; *AW*, ascospore wall; *CC*, conjugation canal; *CM*, cell membrane; *CW*, cell wall; *N*, nucleus; *SW*-1, inner, non-electron dense portion of the ascospore wall; *SW*-2, outer, electron-dense portion of the ascospore wall; *TM*, transverse membrane; *V*, vacuole

portion of the cell wall. The central portion of the connecting wall disintegrates, thereby forming a short, narrow conjugation canal which afterwards increases both in length and width. During this stage the nuclei migrate toward one another and fuse within the canal. The nuclear membrane remains intact except in the region of nuclear fusion. Vacuoles are formed in the majority of cells during or immediately after fusion nucleus formation. The fusion nucleus (presumably diploid) then undergoes a series of divisions resulting in the formation of haploid nuclei (Fig. 1,*p–u*).

Sporulation (Fig. 1,*v*) is initiated by the formation of a double ascospore membrane around each nucleus. The inner portion of the ascospore membrane serves as the structural precursor of the cytoplasmic mem-

brane. The ascospore wall then develops around the outer portion of the ascospore membrane (Fig. 1,*w*). Mature and germinating ascospores are surrounded by two spore coats (Fig. 1,*x*), the inner one giving rise to the vegetative cell wall during germination. Germination is initiated by swelling and elongation of the ascospores with subsequent disruption of the outer spore coat. Vegetative cell division is then initiated.

The results of this study generally support and extend considerably the previous observations on cell division, sporulation, and germination in *S. octosporus*[1–3]. The electron micrographs from which the illustrations are drawn, and a more detailed description of the results will be presented elsewhere.

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BACTERIOLOGY

Antigens of *Azotobacter*

Previous attempts at studying the antigens of *Azotobacter* have met with only limited success. Azo and Yoshida in a brief report[1] described complement-fixation by *Azotobacter* cells in the presence of specific antisera but gave few experimental details. Jensen and Petersen[2] obtained an agglutinating antiserum for *Azotobacter chroococcum*. Recently, Petersen[3] studied the agglutinogens of *Az. chroococcum*, *Az. vinelandii* and *Az. agilis*. *Az. chroococcum* and *Az. vinelandii* had antigens in common and showed serological affinities to *Beijerinckia* sp. *Az. agilis* appeared to be antigenically distinct. Eisenstark *et al.*[4], on the other hand, using apparently adequate technical methods, failed to produce antisera to *Az. agilis* or "numerous other azotobacter species". Heidelberger (quoted in Lawson and Stacey[5]) showed *Az. chroococcum* polysaccharide to be antigenic.

A knowledge of the antigenic structure of *Azotobacter* could be of value in two ways: the genus presents taxonomic problems which may be clarified by a serological study[3] and the large cells are eminently suitable subjects with which to study the distribution of antigens within the cells. Methods are available for the fractionation of these organisms into their structural components[6].

In the present investigation cultures were grown on glucose, nitrogen-free, agar at 30° for two days and harvested into sterile saline. Antisera to *Az. agilis* (V.J.) were prepared by injecting freshly prepared untreated cell suspensions, adjusted to an opacity equal to that of Brown's tube No. 8, intravenously into rabbits. A series of injections consisting of 0·5, 1·0, 2·0, 2·0, 2·0 and 2·0 ml. at 3-day intervals was followed by a rest period of 1 month, after which three further injections of 1·0, 2·0 and 2·0 ml. were given. Antisera were stored without preservative at −20°.

Table 1. Distribution of *Azotobacter agilis* Antigens among Other *Azotobacter* Species

Species (strain)	No. of antigens detected	Known antigens (referred to a standard gel diffusion plate —antigen/antibody lines numbered from the antiserum reservoir outwards)
Az. agilis (V.J.)	5	1 2 3 4 5 (complex)
Az. agilis (4·4)	5	1 2 4 5 (partial)
Az. insigne (V.J.5)	4	2 4
Az. macrocytogenes (0)	4	2 4
Az. chroococcum (222)	1	4
Az. beijerinckii (L.H.1)	2	4
Az. vinelandii (0)	3	4

Antigen–antibody reactions were studied by the Ouchterlony gel diffusion technique. Cells from 2-day old agar cultures were harvested into sterile saline containing 1 in 10,000 thiomersalate and deposited by centrifuging. The deposit was resuspended in a minimal amount of the same medium to give a thick paste of cells which could just be handled conveniently with a Pasteur pipette. The resulting cell suspensions were used as antigen preparations. Sensitivity and resolution of lines were improved by using thin layers of diffusion medium, and after several trials 0·5 ml. amounts of a 1·7 per cent agar/saline base containing 1 in 10,000 thiomersalate in 3¼-in. Petri dishes were chosen as the conditions giving the best results. Antigen suspensions and antisera were accommodated in cork-borer holes, and the Petri dishes were sealed into small plastic bags and incubated at 30°. Although precipitation lines could be seen after 24 hr., the full complement of lines required up to two weeks to develop—presumably some antigens are only slowly released from the cells under these conditions. Fully developed plates were preserved by drying, stained with naphthalene black, and photographed against a yellow safelight screen.

Fig. 1 shows a typical result obtained by allowing antigens from six species of *Azotobacter* to diffuse against *Az. agilis* (V.J.) antiserum. *Az. agilis* (V.J.) has at least five antigens which may be numbered from the antiserum reservoir outwards for reference. One of the antigens (No. 4) has been found in all strains of *Azotobacter* so far studied. The fifth antigen, giving the heaviest line on the plates, is clearly complex and is occasionally seen to consist of numerous components (Fig. 2) some of which are present in other strains of *Az. agilis* (Fig. 3). The details of the distribution by species of all the antigens

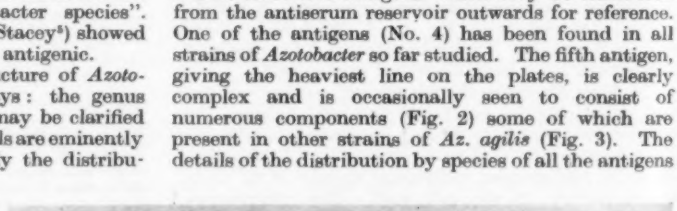

Fig. 1 Fig. 2 Fig. 3

Fig. 1. Gel diffusion plate. Antiserum to *Azotobacter agilis* (V.J.) in the centre. Antigens: 1, *Az. agilis* (V.J.); 2, *Az. insigne* (V.J.5); 3, *Az. vinelandii* (0); 4, *Az. beijerinckii* (L.H.1); 5, *Az. chroococcum* (222); 6, *Az. macrocytogenes* (0)

Fig. 2. Gel diffusion plate. *Az. agilis* (V.J.) antigen diffusing against the homologous antiserum. Photograph showing the complexity of antigen No. 5

Fig. 3. Gel diffusion plate showing the partial sharing of the complex antigen No. 5 between two strains of *Az. agilis*. Antigen suspensions diffusing against *Az. agilis* (V.J.) antiserum

are not yet completely worked out, but Table 1 summarizes the distribution as it is understood at the moment. The suggestion of a close relationship between *Az. agilis*, *Az. insigne* and *Az. macrocytogenes* is of great taxonomic interest. The closeness of *Az. agilis* and *Az. insigne* is well known[7], but the relationships of *Az. macrocytogenes* are not fully understood, although Johnstone[8] has shown that it shares with *Az. agilis* the ability to produce a water-soluble pigment giving a white fluorescence in ultra-violet light. I have noted a similar pigment in *Az. insigne* (unpublished observation).

Antisera active against *Az. chroococcum* have been prepared, and this work is being extended to include antisera to each of the species of *Azotobacter*. Attempts will be made to determine the chemical nature and position within the bacterial cell of some of these antigens, and a fuller report of the work will be published elsewhere.

I am indebted to Dr. J. G. P. Hutchison, of this Department, for advice concerning the drying and staining of gel diffusion plates.

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Culture of *Desulphovibrio desulphuricans*

In a discussion about the method proposed by us[1] for the counting of sulphate-reducing bacteria in mixed population, Dr. J. R. Postgate pointed out in correspondence that, if one is handling a natural sample in which the population of sulphate-reducing bacteria out-numbers that of other micro-organisms, then the higher dilutions of such a sample are effectively pure cultures. Evaluation of our method with pure cultures of *D. desulphuricans* was obviously indicated. Dr. Postgate kindly furnished us with lyophilized pure cultures of the freshwater strain Hildenborough (N.C.I.B. 8303) and the salt-water strain El Agheila *Z* (N.C.I.B. 8380) of *D. desulphuricans*. Our experience in the culturing of both strains from the desiccates is summarized in Table 1; an iron nail in the medium clearly obviates difficulties in the revival of lyophilized cultures and, in addition, makes the exclusion of oxygen unnecessary. In a medium containing a nail, cysteine did not appear to be essential although it promoted earlier growth.

For comparing media for use in determining dilution counts of *D. desulphuricans*, decimal dilutions of a fresh culture in Starkey's medium (*LS*) were prepared in physiological saline, and 1 ml. of each dilution was transferred to each of five tubes of medium being tested. Incubation was at 30° C. for seven days. Some typical results are shown in Table 2. The results did not differ when cysteine hydrochloride (Merck) was included in *LS* + nail before sterilization or as Seitz-filtered solution just prior to inoculation. As autoclaving cysteine in presence of nail not infrequently resulted in slight darkening of the medium,

Table 1. Influence of Medium on Revival of *D. desulphuricans* from Lyophilized Cultures*

Medium†	Anaerobic incubation‡	No. of tubes inoculated	No. of tubes showing growth§	Incubation period at 30° C. (days)
Hildenborough strain				
LSYC	+	2	0	12
LSYC nail	+	3	3	2
LSYC nail	−	3	3	2
LSC nail	+	3	3	2
LSC nail	−	3	3	2
LS nail	+	4	4	3
LS nail	−	2	2	3
El Agheila *Z* strain				
LSYC	+	2	0	9
LSYC nail	+	2	2	2
LSYC nail	−	2	2	2
LSC nail	+	2	2	2
LSC nail	−	2	2	2
LS nail	+	2	2	5
LS nail	−	2	2	8

* Inoculum *c.* 0·05 ml. per tube containing 5 ml. medium.
† *L*, sodium lactate, 3·5 gm./l.; *S*, sodium sulphate, 2 gm./l.; *Y*, yeast extract 'Difco', 1 gm./l.; *C*, cysteine hydrochloride, 1 gm./l. All media contained ammonium chloride, 1 gm.; dipotassium hydrogen phosphate, 0·5 gm.; calcium chloride, 0·1 gm.; Mohr's salt, 0·1 gm.; and tap water to 1,000 ml.; *p*H 7. For El Agheila *Z* strain 25 gm. sodium chloride per litre media were included.
‡ Provided by pyrogallol and sodium carbonate.
§ Indicated by blackening.

it was found advantageous to add the flame-sterilized nail before inoculation. Neither Grossman and Postgate's[2] medium (*LSYC*) nor Starkey's medium containing a nail gave quantitative recoveries of viable bacteria. The inclusion of iron in the first medium or of an aerobic organism such as *Serratia marcescens* or *Aerobacter aerogenes* in the second permitted good growth. Addition of cysteine, yeast extract or peptone to *LS* + nail greatly improved the results. Such favourable effect was not apparent in the absence of nail. This suggests that in the presence of nail, cysteine acted chiefly as a nutrient (cf. Senez and Leroux-Gilleron[3]) rather than by poising the oxidation-reduction potential. The benefits given to aerobes do not seem to be simply due to oxidation-reduction potential changes as they gave occasionally poorer results than media containing cysteine and their effect was not apparent in the absence of nail. A question that requires elucidation is why the organisms in absence of iron nail found difficulty in initiating growth. It looks as if the nail provides an optimal surface for the initiation of growth, as the blackening

Table 2. Growth of *D. desulphuricans* under Different Cultural Conditions

Medium*	Anaerobic incubation	No. of positive tubes at a dilution of 10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	10^{-7}	10^{-8}	10^{-9}
Hildenborough strain										
LSYC	+	5	0	1	0	1	0	0	0	0
LSYC nail	+	5	5	5	5	5	5	5	5	5
LSYC nail	−	5	5	5	5	5	5	5	4	5
LSY nail	−	5	5	5	5	5	5	5	3	1
LSP nail	−	5	5	5	5	5	5	5	5	1
LS nail	−	5	0	0	0	0	0	0	0	0
LS nail	+	5	0	2	2	0	0	0	0	0
LS nail *S. marcescens*	−	5	5	5	5	5	5	5	5	5
El Agheila *Z* strain										
LSYC	+	0	0	0	0	0	0	0	0	0
LSYC nail	+	5	5	4	5	5	4	5	5	4
LSYC nail	−	5	5	3	5	4	5	5	5	2
LSY nail	−	5	5	5	5	5	5	5	2	0
LS nail	−	2	0	0	0	0	0	0	0	0
LS nail	+	3	0	0	0	0	0	0	0	0
LS nail *S. marcescens*	−	5	5	5	5	5	5	4	1	0

* See footnote to Table 1.

in the cultures invariably appeared first on the nail, and once growth is initiated the hydrogen sulphide produced helps the continuity of active multiplication because of its reducing properties. This interpretation finds support in the experiments on corrosion at Teddington in which growth was observed to start on the iron specimen (Postgate, J. R., personal communication).

Three media for dilution counts of *D. desulphuricans* were compared using soil containing a dense population of that species. The soil was prepared by placing 25 gm. of an air-dry, sieved clay loam in a tube, adding 6 ml. of a fresh *LS* culture of the 'Hildenborough' strain, and 6 ml. of sterile *LS* medium; the soil was then incubated anaerobically for 3 days at 30° C. Counts were then made using (*a*) *LS* + nail, (*b*) *LS* + nail, inoculated from one-day agar culture of *Serratia marcescens*, and (*c*) *LSYC* + nail. Results typical of those obtained in three trials appear in Table 3. They indicate that Starkey's medium plus nail is suitable for counting sulphate-reducing bacteria in natural materials containing large numbers of such organisms.

Table 3. Dilution Counts of Dense Populations of *D. desulphuricans* in Soil

Medium*	No. of positive tubes at a dilution of :†								
	10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	10^{-7}	10^{-8}	10^{-9}
LS + nail	5	5	5	5	5	5	3	1	0
LS + nail + *S. marcescens*	5	5	5	5	5	5	3	2	0
LSYC + nail	5	5	5	5	5	3(2)	2(3)	0(5)	0

* See footnote to Table 1.
† Figures in parenthesis indicate false positive tubes.

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GENETICS

Differential Transmission of Gametes in Wheat

One of the basic principles of Mendelian genetics is that union of different gametes takes place at random, and genetic ratios are based on this assumption. In a few species, including *Vigna sinensis* Endb.[1] and *Hordeum vulgare* L.[2], the possibility of differential transmission of alleles has been suggested. The work reported here produces evidence that differential gametic transmission operates in wheat and gives rise to irregular inheritance patterns.

Investigators in Australia and North America have found that the varieties Gabo, Yalta, Charter, Lee and Timstein carry the same resistance to wheat stem rust, *Puccinia graminis* Pers. var. *tritici* (Eriks. and E. Henn.). Reports differ, however, as to the mode of inheritance of resistance. Workers in North America[3], using Chinese Spring as the susceptible variety, found evidence for two linked, dominant, complementary factors governing resistance (*Sr* 11 and *Sr* 12). Monosomic analysis located the two genes on the *X* chromosome, and linkage values of 20–29·5 per cent were proposed. Australian workers[4,5], on the other hand, using crosses with Federation, concluded that a single factor is involved.

Most of the data for this study were obtained from F_2 and F_3 generations of crosses involving the varieties Gabo, Yalta, Charter, Eureka and Mentana. The latter two were used as stem rust susceptible parents. Mentana is resistant to strain 68 *Anz*-3 of wheat leaf rust, *Puccinia triticina* Erikss. Seedling tests with leaf rust were carried out and the plants classified as resistant, intermediate or susceptible. In their reaction to stem rust, plants were clearly either resistant or susceptible.

Failure to obtain susceptible segregates in the F_2 of intercrosses confirms that the varieties Gabo, Yalta and Charter have the same gene or genes for resistance to race 126 of stem rust. In crosses of these three varieties with Eureka a single, dominant gene seemed to segregate. Crosses with Mentana, however, gave results similar to those reported by North American workers. They did not fit a single-factor hypothesis, and in the cross Yalta × Mentana a ratio of approximately 1 : 1 was evident (Table 1).

Table 1

	Resistant	Susceptible	Ratio	Probability (3 : 1)
Gabo × Eureka	462	161	2·9 : 1	0·70–0·50
Charter × Eureka	89	31	2·9 : 1	0·90–0·80
Yalta × Eureka	186	61	3·0 : 1	0·95–0·90
Gabo × Mentana	404	169	2·4 : 1	0·02–0·01
Charter × Mentana	500	226	2·2 : 1	<0·001 (9 : 7)
Yalta × Mentana	467	465	1·0 : 1	<0·001

Similarly, in studies of leaf rust resistance, there was inconsistency in F_2 segregation of crosses involving Mentana and the varieties Eureka, Spica, Kenya 117*A*, Gabo, Charter and Yalta. In the latter cross only a few susceptible F_2 seedlings were found. It was also apparent that the stem rust resistance of Gabo, Yalta and Charter was closely linked with the leaf rust resistance of Mentana. As these resistances entered the crosses in the repulsion phase it was thought possible that the unusual F_2 ratios might be explained by examining F_3 lines (Table 2).

Table 2. Reaction of F_3 Lines of Crosses Gabo × Mentana and Yalta × Mentana to Strains 126 *Anz*-1 of *P. gr. tritici* and 68 *Anz*-3 of *P. triticina*

		Reaction to *P. gr. tritici*					
		Resistant		Segregating		Susceptible	
Reaction to *P. triticina*	Resistant	—	—	—	—	62	107
	Segregating	—	1	121	93	3	2
	Susceptible	40	4	—	1	1	—

First columns, Gabo × Mentana; second columns, Yalta × Mentana.

The results shown in Table 2 cannot be explained on a Mendelian basis. In both crosses close linkage in the repulsion phase between stem rust and leaf rust resistance is evident, and the different segregation ratios in the two crosses indicate that differential transmission of gametes is involved.

A striking feature in the F_2 ratio of the cross Yalta × Mentana was the low proportion of homo-

zygous stem rust resistant lines. This, like the previous F_2 ratio of 1 : 1, could be explained by partial failure of pollen carrying the dominant allele. In many segregating F_2 lines, however, there was a considerable excess of susceptible segregates, and a second test of 14 lines confirmed this behaviour. The actual numbers were 150 resistant to 294 susceptible (χ^2 for a 1 : 1 ratio = 46·703; $P = <0·001$). This indicates that differential transmission operates in the female as well as in the male gametes.

A backcross Mentana × (Yalta × Mentana) tested with stem rust gave 2 resistant and 11 susceptible plants. The two resistant plants, when selfed, gave progeny in a ratio of 2·2 resistant : 1 susceptible instead of the expected 1 : 1. This contradicts the hypothesis that the mode of inheritance of resistance of Yalta is controlled by two or three dominant, complementary factors, as this hypothesis requires that the ratio in backcrosses to Mentana remain constant at 1 : 1.

These studies support the suggestion that there is only one factor for Gabo-type resistance. It is also likely that there is only one major factor for leaf rust resistance in Mentana. The main basis for these assumptions is the relative infrequency of crossing-over in the repulsion phase.

That partial sterility is the cause of these results is improbable. F_1 plants of Mentana crosses show no marked infertility; and the high germinability of the F_2 seeds does not indicate differential zygotic viability.

Further work will be done to find the mechanism causing this departure from random Mendelian segregation. It would also be of interest to determine whether chromosomes other than the *X* chromosome are affected.

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Correlation of Loss of Photoreversibility of Ultra-violet-induced Mutations with Deoxyribonucleic Acid Synthesis

Previous work suggests that nucleic acid precursors altered *in vivo* by ultra-violet light serve as metabolic intermediates for mutation induction in *Escherichia coli*[1]. Other studies indicate that in the absence of an adequate source of nitrogen, an immediate and rapid decline in frequency of mutations induced by ultra-violet light occurs[2,3]. Prevention of this decline depends on the availability of a complex supply of amino-acids immediately following radiation exposure. The potential mutation is modified during post-irradiation incubation so that it is no longer subject to reversal by those agents inhibitory to protein or ribonucleic acid synthesis which cause decline in mutation frequency. Progression of loss of mutation susceptibility to chloramphenicol reversal is closely correlated with the post-irradiation synthesis of ribonucleic acid. Furthermore, experimentation has shown that a relation exists between the amount of post-irradiation ribonucleic acid which has been synthesized at the time of addition of chloramphenicol, the rate of synthesis of deoxyribonucleic acid in the presence of chloramphenicol, and the induced mutation frequency response obtained at subsequent plating[4]. These results suggest that ribonucleic acid and protein syntheses are required for mutation induction and synthesis of deoxyribonucleic acid following exposure to ultra-violet light. It would appear that only those cells which have synthesized the ribonucleic acid and protein necessary for genetic replication prior to addition of chloramphenicol are able to reproduce their deoxyribonucleic acid and thereby acquire mutant characters.

Recent studies of mutation expression have yielded further information on the relation of mutation induction to synthesis of deoxyribonucleic acid[5]. Mutation expression closely follows the initial net synthesis of deoxyribonucleic acid in irradiated cultures. Since chloramphenicol treatment subsequent to synthesis of deoxyribonucleic acid blocks this expression, protein synthesis following synthesis of the acid must take place in order for the induced mutations to be phenotypically expressed. The experiments we wish to report here relate to the involvement of synthesis of deoxyribonucleic acid in the mutation-induction process. These studies demonstrate that loss of photoreversibility of ultra-violet-induced mutation is closely correlated with post-irradiation synthesis of deoxyribonucleic acid.

The mutations studied result in reversion to the prototrophic state in *E. coli* strain *WP2* (a tryptophan-

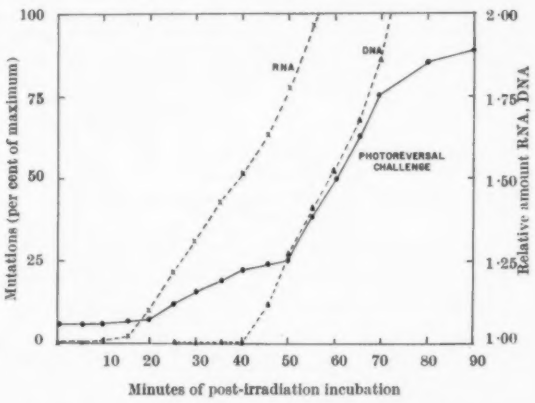

Fig. 1. The effect of challenge by photo-reversing light at increasing post-irradiation incubation intervals on the yield of ultra-violet-induced prototrophs from *Escherichia coli* strain *WP2*. Mutations are expressed as the percentage of those appearing in ultra-violet-irradiated control cultures which were incubated for an identical time interval and held for 1 hr. in an ice bath in the dark prior to plating. Photoreversal was carried out by subjecting ultra-violet-irradiated cultures to the light emitted by two 500-watt General Electric projection lamps. These were located 6 in. from the culture samples which were in small test-tubes immersed in an ice bath. The samples were exposed to the photo-reversing light for 1 hr., an exposure period which has been shown to produce maximum photoreversal. The incubation medium was minimal medium (ref. 1) plus casein hydrolysate (2 mgm./ml.) and DL-tryptophan (0·02 mgm./ml.). Ultra-violet exposure was 960 ergs/mm.^{2}. Induced mutation frequency response for unphotoreversed cells was approximately 8,000 prototrophs per 10^8 surviving organisms and did not vary significantly with incubation over a 90-min. period. Plating was on mutation assay agar previously described (see Doudney and Haas, ref. 3). Survival following this dose of ultra-violet radiation was approximately 50 per cent. The white light treatment resulted in photoreactivation to the 70 per cent level of survival when applied without incubation. This effect was lost by 20 min. incubation. The cultures during incubation contained about 10^8 bacteria per ml. (as determined by colony formers observed with plating prior to radiation exposure)

requiring auxotroph isolated by Witkin). The procedures for culture growth, synchronization, radiation exposure, post-irradiation treatment, plating and mutation assay have been described, as have the procedures used for nucleic acid determination[1–3].

The loss of susceptibility of ultra-violet-induced mutations to photoreversal with post-irradiation incubation has been demonstrated with several systems[4–11] and a similar effect with the tryptophan reversion used here has been described[3]. Fig. 1 demonstrates that approximately 20 per cent of the potential mutations lose their capacity to be photoreversed prior to net measurable synthesis of deoxyribonucleic acid in the culture. However, the larger portion of potential mutations lose this capacity in correlation with synthesis of deoxyribonucleic acid. At the time that deoxyribonucleic acid has doubled (70 min.) approximately 80 per cent of the mutations are no longer susceptible to photoreversal.

Two processes may be involved in this loss of susceptibility to photoreversal. The initial process may represent some physical or chemical conversion of the radiation-modified factor responsible for the induction of the mutation to a non-photosensitive state prior to synthesis of deoxyribonucleic acid. However, the loss of susceptibility to photoreversal which is correlated with synthesis of deoxyribonucleic acid would seem to be due to actual synthesis of the mutated gene. These results therefore support the hypothesis that ultra-violet-induced mutation involves finally the synthesis of deoxyribonucleic acid following ultra-violet exposure[5].

These preliminary studies will be reported more fully elsewhere. This research was supported in part by research grant *C*-3323 from the United States National Institutes of Health and by U.S. Atomic Energy Commission Contract *AT*-(40-1)-2139.

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SOIL SCIENCE

Symbiotic Nitrogen Fixation in a Grazed Tropical Grass–Legume Pasture

The importance of legumes as symbiotic nitrogen-fixers in the pastures of temperate regions is generally recognized, and considerable data are available to show the contributions made to the soil nitrogen supply by these legumes. Very little information of this nature, however, is available in the case of legumes growing in tropical pastures. Tropical legumes are often considered to be inefficient nitrogen-fixers; in instances where this is so, it is probable that inoculation with the appropriate *Rhizobium* strain or the supplying of deficient nutrients, or both, will increase fixation efficiency. Results obtained from an experiment on the Faculty of Agriculture Farm, University College, Ibadan, indicate that under suitable conditions the legume in a pasture growing under equatorial conditions may contribute amounts of nitrogen to the soil similar to those added by legumes in temperate pastures.

A grazing experiment comparing the productivity of a pure grass stand (*Cynodon plectostachyum*) and a mixed pasture (*Cynodon plectostachyum–Centrosema pubescens*) was established in mid-1953 and terminated in mid-1958. The soil of the experimental area was a latosol, Ibadan loamy coarse sand. On inspection the roots of the *Centrosema* were found to be well nodulated. The colour of the grass in the mixed pasture was a much darker green than that of the pure grass plot, suggesting that there were significant soil nitrogen differences between these plots. In September 1958 the plots were sampled to a depth of 12 in. and total (Kjeldahl) nitrogen of the samples determined. These nitrogen contents are shown in Table 1; to express the values in lb. per acre it was assumed that an acre-6-in. of soil weighed 2 million lb.

Table 1. Soil Nitrogen (Kjeldahl) under Five-Year-Old Grazed Pure Grass and Grass–Legume Pastures at University College, Ibadan, Nigeria

Depth (in.)	Soil nitrogen under *Cynodon plectostachyum* and *Centrosema pubescens* (lb. per acre)	Soil nitrogen under *Cynodon plectostachyum* (lb. per acre)	Difference in soil nitrogen (lb. per acre)
0–2	770	510	260
2–4	460	370	90
4–8	770	610	160
8–12	600	550	50
0–12 (Total)	2,600	2,040	560*

Each value is the mean of three replicates.
* '*t*' test : $P = 0{\cdot}10$.

There were 560 lb. of nitrogen per acre-ft. more in the soil under grass–legume than in the soil under grass. This was a net gain over a five-year period and may reasonably be attributed to symbiotic nitrogen fixation by the *Centrosema*. On an average annual basis the *Centrosema* had fixed 112 lb. of nitrogen per acre-ft. Thus the average annual increment of soil nitrogen due to *Centrosema* in this tropical mixed pasture was of the same order of magnitude as those for temperate pasture legumes. For example, Russell[1] states that clovers and lucerne may add to the soil 150–200 lb. of nitrogen per acre per year.

It appears that, under suitable conditions, pasture legumes may play as important a part in the nitrogen economy of tropical soils as they do in the case of temperate soils.

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[1] Russell, E. J., "Soil Conditions and Plant Growth", 323 (Longmans, Green and Co., London, 1950).

FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, February 29

UNIVERSITY OF LONDON (in the Physiology Theatre, University College, Gower Street, London, W.C.1), at 5 p.m.—Dr. Antoinette Pirie: "The Biochemistry of the Eye".* (Further lecture on March 7).

BRITISH SOCIETY FOR THE HISTORY OF SCIENCE (in the Lecture Theatre of the Science Museum, Exhibition Road, South Kensington, London, S.W.7), at 5.30 p.m.—Dr. W. Cameron Walker: "Foundations of Current Electricity and Electro-Chemistry".

SOCIETY OF CHEMICAL INDUSTRY, SURFACE ACTIVITY GROUP (at 14 Belgrave Square, London, S.W.1), at 5.30 p.m.—Dr. E. G. Cockbain: "The Colloidal Stability of Natural Rubber Latex".

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 8.30 p.m.—Mr. A. J. Cain: "The Oxford University Expedition to British Guiana".

Tuesday, March 1

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 1.15 p.m.—Dr. A. J. Arkell: "An Archæologist Visits the Belgian Congo".*

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND CONTROL SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Scientific Papers.

ROYAL SOCIETY OF MEDICINE, PATHOLOGY SECTION (at 1 Wimpole Street, London, W.1), at 5.30 p.m.—Prof. L. S. Penrose, F.R.S.: "Human Genetics and Disease"; Dr. H. Lehmann: "Familial Deficiency of Pseudocholinesterase"; Dr. A. Holzel: "Galactosæmia—a Hereditary Disease".

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. A. Isaacs: "The Anti-Viral Action of Interferon". (Last of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)*

INSTITUTION OF MECHANICAL ENGINEERS, AUTOMOBILE DIVISION (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Mr. Wheeler G. Lovell: "The Chemistry of Future High-Compression Engines" (James Clayton Lecture).

UNIVERSITY OF LONDON (in the Beveridge Hall, Senate House, London, W.C.1), at 6 p.m.—Sir Douglas Logan: Birkbeck College Haldane Memorial Lecture.

PLASTICS INSTITUTE (at the Wellcome Building, 183–193 Euston Road, London, N.W.1), at 6.30 p.m.—Dr. N. Grassie: "Recent Investigations into Polymer Degradation".

SOCIETY OF CHEMICAL INDUSTRY, PLASTICS AND POLYMER GROUP (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Dr. A. Keller: "Some New Aspects of the Crystallization of High Polymers".

Wednesday, March 2

ROYAL SOCIETY OF ARTS (at John Adam Street, Adelphi, London, W.C.2), at 2.30 p.m.—Mr. F. I. G. Rawlins: "Scientific Methods in the Care of Works of Art".

INSTITUTE OF PETROLEUM (at 61 New Cavendish Street, London, W.1), at 5.30 p.m.—Mr. Michel Estavoyer: "Corrosion Problems in the Lacq Field".

ROYAL METEOROLOGICAL SOCIETY (at 49 Cromwell Road, London, S.W.7), at 5.30 p.m.—Dr. H. L. Penman: "Weather, Soil and Plant Factors in Hydrology".

UNIVERSITY OF LONDON (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. G. Schramm (Tübingen): "Mutagenesis in Viruses".*

INSTITUTION OF MECHANICAL ENGINEERS, NUCLEAR PANEL (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Discussion on "The Role of Formal Education and Training in Nuclear Power Developments".

Thursday, March 3

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 10.30 a.m.—Discussion on "Problems of Stellar Evolution", opened by Prof. F. Hoyle, F.R.S.

INSTITUTE OF REFRIGERATION (at the Institute of Marine Engineers, The Memorial Building, 76 Mark Lane, London, E.C.3), at 5.30 p.m.—Dr. E. Baumgartner: "European Refrigerated Transport by Railway".

INSTITUTION OF ELECTRICAL ENGINEERS (joint meeting with the INSTITUTIONS OF CIVIL and of MECHANICAL ENGINEERS, at Savoy Place, London, W.C.2), at 5.30 p.m.—Sir Hugh Beaver, K.B.E.: "The Engineer and Civilization" (Sixth Graham Clark Lecture).

BRITISH PSYCHOLOGICAL SOCIETY, EDUCATION SECTION (in the University of London Institute of Education, Malet Street, London, W.C.1), at 6.15 p.m.—Annual General Meeting. Prof. Allen L. Edwards (U.S.A.): "The Effects of Social Desirability upon Personality Measurement".

Friday, March 4

ZOOLOGICAL SOCIETY OF LONDON (at Regent's Park, London, N.W.1), at 10.15 a.m.—Symposium on "Sensory Specialization in Response to Environmental Demands".

LINNEAN SOCIETY OF LONDON (joint meeting with the SYSTEMATICS ASSOCIATION, at Burlington House, Piccadilly, London, W.1), at 10.45 a.m.—Symposium on "The Subspecies". Speakers include Prof. Valentine, Dr. Hawkes, Dr. Warburg, Mr. Ross, Dr. Galbraith, Dr. Clay, Mr. Stroyan and Dr. de Wolf.

ROYAL ASTRONOMICAL SOCIETY (joint meeting with the ROYAL METEOROLOGICAL SOCIETY, at the Royal Society of Arts, John Adam Street, London, W.C.2), at 2.30 p.m.—Geophysical Discussion on "The British Rocket Programme". Chairman: Prof. Sir H. S. W. Massey, F.R.S.).

INSTITUTION OF ELECTRICAL ENGINEERS, MEDICAL ELECTRONICS DISCUSSION GROUP (at Savoy Place, London, W.C.2), at 6 p.m.—Discussion on "Direct Writing Oscillographs" opened by Mr. A. Smale and Mr. S. N. Pocock.

SOCIETY OF DYERS AND COLOURISTS (at the Northampton College of Technology, St. John Street, London, E.C.1), at 6 p.m.—Mr. J. H. Sharphouse: "Recent Developments in Leather Dyeing".

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—Sir Charles Darwin, K.B.E., F.R.S.: "Some Episodes in Darwin's Voyage on 'The Beagle'".

Saturday, March 5

BRITISH INTERPLANETARY SOCIETY (in the Lancaster Room, Caxton Hall, Westminster, London, S.W.1), at 2.30 p.m.—Symposium on "The Exploration of the Moon".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

ASSISTANT LECTURER (preferably with research interest in polymer chemistry, carbonyls or high-pressure reactions) IN ORGANIC CHEMISTRY—The Registrar, The Manchester College of Science and Technology, Manchester 1 (March 5).

LECTURER IN THE PHILOSOPHY OF SCIENCE—The Secretary, The University, 38 North Bailey, Durham (March 7).

LECTURER IN PHYSICAL CHEMISTRY; and an ASSISTANT LECTURER IN ZOOLOGY—The Registrar, Queen Mary College (University of London), Mile End Road, London, E.1 (March 8).

SENIOR SCIENTIFIC OFFICER, PHYSICAL CHEMIST (with a first- or second-class honours degree or equivalent) at Warren Spring Laboratory, D.S.I.R., Stevenage, Herts, for work on electrochemistry of surface and colloidal reactions, forming part of a programme of research on fundamentals of froth flotation and mineral processing—The Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting Ref. F.79/0A (March 11).

ASSISTANT LECTURERS (2) (interested in plant biochemistry, experimental work with marine algae or genetics) IN BOTANY; a LECTURER or ASSISTANT LECTURER IN INORGANIC CHEMISTRY; an ASSISTANT LECTURER IN PHYSICAL CHEMISTRY; and an ASSISTANT LECTURER IN ORGANIC CHEMISTRY; an ASSISTANT LECTURER IN GEOGRAPHY; an ASSISTANT LECTURER IN PURE MATHEMATICS and an ASSISTANT LECTURER IN APPLIED MATHEMATICS; a SENIOR LECTURER IN PHYSICS; an ASSISTANT LECTURER IN VERTEBRATE EMBRYOLOGY and an ASSISTANT LECTURER IN INVERTEBRATE ZOOLOGY—The Registrar, The University, Hull (March 12).

CURATOR OF THE GULBENKIAN MUSEUM OF ORIENTAL ART AND ARCHÆOLOGY—The Secretary, The University, 38 North Bailey, Durham (March 12).

HOSPITAL PHYSICIST, Basic or Senior grade (preferably with a knowledge of radiotherapy)—The House Governor, King's College Hospital, Denmark Hill, London, S.E.5 (March 12).

LECTURER (preferably with industrial experience or an interest in applied physical chemistry) IN PHYSICAL CHEMISTRY in the Department of Applied Chemistry—The Secretary, Northampton College of Advanced Technology, St. John Street, London, E.C.1 (March 12).

LECTURER, TERMINABLE LECTURERS, and an ASSISTANT IN THE DEPARTMENT OF MATHEMATICS—The Secretary, The University, Aberdeen (March 12).

ASSISTANT LECTURER IN PHYSICS—The Secretary and Registrar, University College of North Wales, Bangor, North Wales (March 15).

LECTURER (with a special interest in one or more of the following fields: soils, conservation, or land use) IN GEOGRAPHY—The Secretary, University College, Gower Street, London, W.C.1 (March 15).

LECTURER (preferably with a special interest in semi-conductors and their applications) IN APPLIED PHYSICS—The Secretary, The University, 38 North Bailey, Durham (March 18).

ASSISTANT LECTURER IN ENDOCRINE BIOCHEMISTRY, to work in the University Endocrine Unit at the Liverpool Radium Institute—The Registrar, The University, Liverpool, quoting Ref. CV/T (March 19).

LECTURER (with some experience in microscopic anatomy or electron microscopy) IN ANATOMY—Joint Clerk to the University Court, Queen's College (University of St. Andrews), Dundee (March 19).

LECTURER or ASSISTANT LECTURER (with special qualifications in palæontology or stratigraphy) IN GEOLOGY—The Registrar, The University, Sheffield (March 19).

LECTURER IN PSYCHOLOGY—The Secretary, The Queen's University, Belfast (March 21).

LECTURER IN PHYSICS at the University of Cape Town, South Africa—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (South Africa, March 22).

CHAIR OF METALLURGY—The Registrar, University College of South Wales and Monmouthshire, Cathays Park, Cardiff (March 26).

LECTURER IN BOTANY—The Secretary, The University, 38 North Bailey, Durham (March 26).

LECTURER (with research experience in physical oceanography or in an appropriate branch of physics or mathematics) IN PHYSICAL OCEANOGRAPHY—The Secretary and Registrar, University College of North Wales, Bangor, North Wales (March 29).

RESEARCH FELLOW (with research experience in biochemistry or chemistry and interest in the physico-chemical aspects of biochemistry) IN THE DEPARTMENT OF PHYSICAL BIOCHEMISTRY, John Curtin School of Medical Research, Australian National University—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (March 30).

CHAIR OF MEDICINE tenable at Charing Cross Hospital Medical School—The Academic Registrar, University of London, Senate House, London, W.C.1 (March 31).

LECTURER or SENIOR LECTURER (with research experience in statistics) IN MATHEMATICS—The Secretary, The University, 36 North Bailey, Durham (March 31).

LECTURER IN PSYCHOLOGY at the University of Adelaide, Australia —The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, March 31).

PRINCIPAL (with high academic qualifications and appropriate educational and administrative experience) OF THE NORTHERN POLYTECHNIC—R. H. Currell, F.C.A., Northern Polytechnic, Holloway, London, N.7 (March 31).

SENIOR LECTURER IN THEORETICAL PHYSICS at the University of Cape Town, South Africa—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (South Africa, March 31).

READER IN PHYSIOLOGY at King's College, Strand, London, W.C.2 —The Academic Registrar, University of London, Senate House, London, W.C.1 (April 1).

READER IN MATHEMATICS at King's College, Strand, London, W.C.2—The Academic Registrar, University of London, Senate House, London, W.C.1 (April 4).

ELECTRON MICROSCOPIST IN THE DEPARTMENT OF PHYSICAL BIOCHEMISTRY, John Curtin School of Medical Research, Australian National University—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, April 18).

HEAD (with a good honours degree, preferably in physics or chemistry, experience of teaching and examinations at G.C.E. advanced level and also at degree level) of the Department of Science, Zaria Branch, Nigerian College of Arts, Science and Technology—The Council for Overseas Colleges, 12 Lincoln's Inn Fields, London, W.C.2 (April 29).

LECTURER IN PHYSIOLOGY (HISTOLOGY)—The Secretary of University Court, The University, Glasgow (April 30).

ACADEMIC REGISTRAR (graduate in science or arts, with teaching, industrial and administrative experience, and preferably knowledge of the work of a major technical college)—The Principal, College of Science and Technology, Ashley Down, Bristol 7.

ASSISTANT CLINICAL BIOCHEMIST (basic grade)—The Group Secretary, Booth Hall Children's Hospital, Blackley, Manchester 9.

BIOCHEMIST TO WORK IN THE ENDOCRINE LABORATORY, Obstetric Unit, mainly on steroids—The Secretary, University College Hospital Medical School, University Street, London, W.C.1.

CHEMIST (with a good honours degree in chemistry or equivalent professional qualification, and preferably specialization or experience in public analyst work) IN THE GOVERNMENT CHEMIST'S DEPARTMENT, Tanganyika, for general analytical work in the fields of toxicology, food and drugs, and water, and the supervision of assistants—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.117/8/037.

GRADUATE (with a knowledge of animal nutrition and/or agricultural chemistry) AT THE ANIMAL HEALTH TRUST FARM LIVESTOCK RESEARCH CENTRE, Stock, Essex, to assist in biochemical investigations—The General Secretary, Animal Health Trust, 14 Ashley Place, London, S.W.1.

LECTURER (preferably with university teaching experience and an active research interest) IN BOTANY—The Registrar, Queen Mary College (University of London), Mile End Road, London, E.1.

LECTURER (qualified to teach botany to B.Sc. and Diploma in Technology level, and preferably special qualifications in plant physiology or plant biochemistry) IN BOTANY—The Registrar, Bradford Institute of Technology, Bradford 7.

STATISTICIAN (with an honours degree in statistics or in mathematics with a diploma in statistics, and interested in the field of physiology) AT THE MEDICAL RESEARCH COUNCIL CLIMATE AND WORKING EFFICIENCY UNIT, Oxford—The Secretary, M.R.C. Unit, Department of Human Anatomy, South Parks Road, Oxford.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Department of Scientific and Industrial Research. Road Research 1958: The Report of the Road Research Board with the Report of the Director of Road Research. Pp. iv+83+4 plates. (London: H.M. Stationery Office, 1959.) 5*s*. 6*d*. net. [2212

Mental Health Research Fund. Supplement Report and Balance Sheet with Income and Expenditure Account for the period from 1st October 1958 to 31st March 1959. Pp. 14. (London: Mental Health Research Fund, 1959.) [2212

National Research Development Corporation. Report and Statement of Accounts for the year 1st July, 1958 to 30th June, 1959. Pp. ii+22. (London: H.M. Stationery Office, 1959.) 1*s*. 3*d*. net. [2212

Final Act of the Conference on Antarctica together with the Antarctic Treaty. Pp. 12. (Cmnd. 913.) (London: H.M. Stationery Office, 1959.) 9*d*. net. [2212

The North Staffordshire Field Club. Transactions and Annual Report, 1957–58. (Vol. XCII.) Edited by H. V. Thompson. Pp. 71+1 plate. (Stoke-on-Trent: North Staffordshire Field Club, 1959.) 15*s*. [2212

Bulletins of Marine Ecology (formerly Hull Bulletins of Marine Ecology). Vol. 4 (November, 1959): Title Page; Contents; List of Personnel; and Explanation by Dr. G. T. D. Henderson. Pp. i–xiii. (Edinburgh: Scottish Marine Biological Association, 1959.) 5*s*. [2212

Other Countries

United States Department of the Interior: Geological Survey. Bulletin 1056–B: Index to the Geologic Names of North America. By D. Wilson, G. C. Keroher and Blanche E. Hansen. Pp. iv+407–622. 60 cents. Bulletin 1058–F: Geology and Coal Resources of the Homer District, Kenai Coal Field, Alaska. By Farrell F. Barnes and Edward H. Cobb. Pp. iv+217–260+plates 17–28. Bulletin 1072–F: Mineral Occurrences of New York State with selected references of Each Locality. By Elaine M. Luedke, Chester T. Wrucke and John A. Graham. Pp. iii+385–444+plate 9. Bulletin 1077: Geology of the Lake Mary Quadrangle, Iron County, Michigan. By Richard W. Bayley. Pp. v+112+7 plates. Bulletin 1081–B: Stratigraphy of the Inyan Kara Group in the Black Hills. By Karl M. Waagé. Pp. iii+11–90+plate 2. 40 cents. Bulletin 1092: Stratigraphy of Middle Tertiary Rocks in Part of West-Central Florida. By Wilfred J. Carr and Douglas C. Alverson. Pp. iv+111+3 plates. 1.25 dollars. Bulletin 1097–B: Lead-Alpha Age Determinations of Accessory Minerals of Igneous Rocks (1953–1957). By Howard W. Jaffe, David Gottfries, Claude L. Waring and Helen W. Worthing. Pp. iii+65–148. 30 cents. Bulletin 1107–A: Bibliography of U.S. Geological Survey Reports on Uranium and Thorium, 1942 through May 1958. By Paul E. Soister and Dora R. Conklin. Pp. v+167. 50 cents. Bulletin 1094: Geology of Possible Petroleum Provinces in Alaska. By Don J. Miller, Thomas G. Payne and George Gray. Pp. v+131+3 plates. 2 dollars. (Washington, D.C.: Government Printing Office, 1959.) [3012

United States Department of the Interior: Geological Survey. Water-Supply Paper 1309: Compilation of Records of Surface Waters of the United States through September 1950. Part 6–A: Missouri River Basin above Sioux City, Iowa. Prepared under the direction of J. V. B. Wells. Pp. v+672+1 plate. Water-Supply Paper 1320–D: Floods of January 1953 in Western Oregon and Northwestern California. By S. E. Rantz. Pp. v+321–339. Water-Supply Paper 1511: Surface Water Supply of the United States 1957. Part 7: Lower Mississippi River Basin. Prepared under the direction of J. V. B. Wells. Pp. xi+527. 1.75 dollars. Water-Supply Paper 1515: Surface Water Supply of the United States 1957. Part 2: Pacific Slope Basins in California. Prepared under the direction of J. V. B. Wells. Pp. xiii+634. 2 dollars. Water-Supply Paper 1542–A: Flow-Duration Curves. By James K. Searcy. (Manual of Hydrology: Part 2—Low-Flow Techniques.) Pp. iv+33. 20 cents. Water-Supply Paper 1459–A: Survey of Ferrous-Ferris Chemical Equilibria and Redox Potentials. By J. D. Hem and W. H. Cropper. Pp. iii+31. 15 cents. Water-Supply Paper 1483: Geology and Ground-Water Resources of the Upper Lodgepole Creek Drainage Basin, Wyoming. By L. J. Bjorklund. Pp. iv+40+2 plates. (Washington, D.C.: Government Printing Office, 1959.) [3012

United States Department of the Interior: Geological Survey. Professional Paper 317–A: Geology of the San Juan Metropolitan Area, Puerto Rico. By Clifford A. Kaye. Pp. ix+48+9 plates. Professional Paper 317–B: Shoreline Features and Quaternary Shoreline Changes, Puerto Rico. By Clifford A. Kaye. Pp. v+49–140+plates 1, 10 and 11. 1.50 dollars. Professional Paper 320: Geochemistry and Mineralogy of the Colorado Plateau Uranium Ores. By Robert M. Garrels and Esper S. Larsen. Pp. v+236+8 plates. 2 dollars. (Washington, D.C.: Government Printing Office, 1959.) [3012

Tea Research Institute of East Africa. Annual Report for the year 1958. Pp. 49+1 plate. (Nairobi: Tea Research Institute of East Africa, 1959.) [3012

Publicaciones del Instituto Antituberculoso "Francisco Moragas" de la Caja de Pensiones para la Vejez y de Ahorros. Volumen XIII: La Extrana Biologia de las Plaquetas Sanguineas (Cultivos *in vitro*). By Dr. C. Xalabarder. Pp. 94 (64 figures). (Barcelona: Instituto Antituberculoso "Francisco Moragas", 1959.) [3012

Metropolitan Life Insurance Company. Statistical Bulletin, Vol. 40 (October 1, 1959): Rapid Suburban Population Growth; Hearing Impairment is Common; Mortality and Social Class. Pp. 12. (New York: Metropolitan Life Insurance Company, 1959.) [3012

Western Australia. Report of the Geological Survey Branch for the year 1957. Pp. 7. (Extract from the Report of the Department of Mines.) (Perth: Government Printer, 1959.) [3012

Comptes Rendus des Traveaux du Laboratoire Carlsberg. Vol. 31, No. 14: Delayed Division in Tetrahymena Pyriformis Induced by Temperature Changes. By H. Thormar. Pp. 207–226. 2 Kr. 60 øre. Vol. 31, No. 15: Appearance of New N-terminal Residues Upon Treatment of Human and Bovine Serum Albumin with N-bromosuccinimide. By T. Peters, Jr. Pp. 227–235. 1 kr. 70 øre. Vol. 31, No. 16: Deuterium Exchange Studies of Sperm Whale Metmyoglobin. Pp. 235–249. 2 kr. 25 øre. Vol. 31, No. 17: Some Observations on Pentose Utilization by *Candida tropicalis*. By Helena Karczewska. Pp. 251–258. 1 kr. 50 øre. (Copenhague: Danish Science Press, Ltd. 1959.) [3012

Bureau des Longitudes. Annuaire pour l'An 1960, publié par le Bureau des Longitudes. Pp. viii+692+4 planches. (Paris: Gauthier-Villars, 1959.) [3012

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